Research To Practice: Adjuvant Chemotherapy

28TH ANNUAL
San Antonio Breast Cancer Symposium 12

Clinical decisions regarding adjuvant chemotherapy are complex and multifactorial. Tumor-related factors such as nodal status, tumor size and predictors like the Onco*type* DX™ assay must be balanced against issues such as patient age and comorbidities. Computer models, such as Peter Ravdin's Adjuvant! Online program, are frequently utilized by oncologists to assist in estimating the absolute impact of adjuvant therapy, and these must be balanced against the risk of side effects and toxicities with treatment. An important facet of Adjuvant! is that it factors in nonbreast cancer sources of competing mortality based on the patient's age and general health status. Data from the 2005 *Breast Cancer Update* Patterns of Care Study, a telephone survey of randomly selected US-based medical oncologists, are presented here. In patients with node-positive tumors, dose-dense AC → paclitaxel is a common choice, but many other regimens are also utilized. AC is the most common regimen utilized in patients with node-negative tumors. Adjuvant chemotherapy is less frequently utilized in older patients, particularly octogenarians.

USE OF COMPUTER MODELS IN CLINICAL PRACTICE

In which of the following situations do you tend to use computer models* to estimate breast cancer patients' risk of relapse and/or mortality? (percent of physicians who use a computer model)	
To review risk estimates with patients	100%
To decide whether to use chemotherapy in node-negative cases	81%
To decide whether to use endocrine therapy in node-negative cases	25%
To select type of chemotherapy to use	34%
To select type of endocrine therapy to use	9%
Other situations	0%

* 44% percent of oncologists surveyed use the Adjuvant! model, 2% use the Mayo clinic model, 18% use both models, and 36% of physicians do not use either model.

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

CLINICAL USE OF ONCO*TYPE* DX ASSAY

Have you ordered the Onco*type* DX assay?	
Yes	34%
No	66%
If you have ordered this assay, in how many patients?	Median = 2
How helpful was this test in your treatment decisions? (N = 17)	
Very helpful	18%
Somewhat helpful	64%
Not helpful	18%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

ADJUVANT CHEMOTHERAPY FOR NODE-NEGATIVE DISEASE

The patient is a woman in average health with a 1.2-cm, ER/PR-positive, HER2-negative (as confirmed by FISH), Grade II tumor and negative lymph nodes. Which chemotherapy regimen, if any, would you most likely recommend for this patient?

	Age 35	Age 55	Age 75	Age 85
AC x 4 q3wk	44%	34%	10%	4%
AC x 4 q2wk	12%	10%	6%	—
FAC or FEC x 6	6%	6%	2%	—
AC x 4 → paclitaxel x 4 q3wk	4%	2%	—	—
AC x 4 → paclitaxel x 4 q2wk	10%	8%	2%	—
AC x 4 → docetaxel x 4 q2wk	10%	4%	2%	—
CMF	8%	8%	10%	10%
TAC (docetaxel) x 6	2%	—	—	—
Other	2%	4%	—	—
No chemotherapy	2%	24%	68%	86%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

ADJUVANT CHEMOTHERAPY FOR NODE-POSITIVE DISEASE

The patient is a woman in average health with a 1.2-cm, ER/PR-positive, HER2-negative (as confirmed by FISH), Grade II tumor and three positive lymph nodes. Which chemotherapy regimen, if any, would you most likely recommend for this patient?

	Age 35	Age 55	Age 75	Age 85
AC x 4 q3wk	4%	4%	14%	—
AC x 4 q2wk	—	—	2%	2%
FAC or FEC x 6	—	—	6%	2%
AC x 4 → paclitaxel x 4 q3wk	6%	6%	6%	—
AC x 4 → paclitaxel x 4 q2wk	44%	44%	14%	2%
AC x 4 q3wk → paclitaxel qwk x 12	4%	8%	8%	2%
AC x 4 → docetaxel x 4 q3wk	2%	4%	8%	—
AC x 4 → docetaxel x 4 q2wk	18%	18%	6%	2%
CMF	—	—	18%	8%
TAC (docetaxel) x 6	22%	16%	2%	2%
Other	—	—	2%	2%
No chemotherapy	—	—	14%	78%

SOURCE: *Breast Cancer Update* Patterns of Care Survey, September 2005. (n = 50)

SELECT PUBLICATIONS

Budman DR. **Dose and schedule as determinants of outcomes in chemotherapy for breast cancer.** *Semin Oncol* 2004;31(6 Suppl 15):3-9.

Campos SM. **Evolving treatment approaches for early breast cancer.** *Breast Cancer Res Treat* 2005;89(Suppl 1):1-7.

Citron ML et al. **Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741.** *J Clin Oncol* 2003;21(8):1431-9.

Di Leo A et al. **Controversies in the adjuvant treatment of breast cancer: The role of taxanes.** *Ann Oncol* 2004;15(Suppl 4):iv17-21.

Henderson IC et al. **Improved outcomes from adding sequential paclitaxel but not from escalating doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer.** *J Clin Oncol* 2003;21(6):976-83.

Mamounas EP et al. **Paclitaxel after doxorubicin plus cyclophosphamide as adjuvant chemotherapy for node-positive breast cancer: Results from NSABP B-28.** *J Clin Oncol* 2005;23(16):3686-96.

Mano MS et al. **Adjuvant anthracycline-based chemotherapy for early breast cancer: Do the dose and schedule matter?** *Cancer Treat Rev* 2005;31(2):69-78.

Martin M et al. **Adjuvant docetaxel for node-positive breast cancer.** *N Engl J Med* 2005;352(22):2302-13.

Nowak AK et al. **Systematic review of taxane-containing versus non-taxane-containing regimens for adjuvant and neoadjuvant treatment of early breast cancer.** *Lancet Oncol* 2004;5(6):372-80.

Olivotto IA et al. **Population-based validation of the prognostic model Adjuvant! for early breast cancer.** *J Clin Oncol* 2005;23(12):2716-25.

Paik S et al. **A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer.** *N Engl J Med* 2004;351(27):2817-26.

Vogel CL et al. **First and subsequent cycle use of pegfilgrastim prevents febrile neutropenia in patients with breast cancer: A multicenter, double-blind, placebo-controlled phase III study.** *J Clin Oncol* 2005;23(6):1178-84.

*ONCO*TYPE *DX AND COMPUTERIZED RISK MODELS*

Peter Ravdin notes that in the Adjuvant! program, the relative benefit of chemotherapy is presumed to be equal for patients at higher and lower risk, but it's likely that the estimation of chemotherapy benefit in the group with low-risk disease is an overestimation. Conversely, the benefit in the group with higher-risk disease may be underestimated. I believe our studies with Onco*type* DX demonstrate this, and Ravdin's model may need to be modified slightly. My prediction is that when people see these data from NSABP-B-20, they will want the assay performed because nobody wants to receive chemotherapy when it will not work.

— Soonmyung Paik, MD.* Breast Cancer Update *2005 (3)

CHEMOTHERAPY AND RECEPTOR STATUS

The estrogen and progesterone receptor status may be important in determining the potential benefit from adjuvant chemotherapy. SWOG-8814 demonstrated that patients with highly ER- and PR-positive tumors received no benefit from FAC chemotherapy. Similarly, data from the Ludwig group showed that highly endocrine-responsive patients received little or possibly no benefit from chemotherapy. Finally, Don Berry's analysis of a series of CALGB/Intergroup studies suggested little or no additional benefit for taxanes added to AC or for dose-dense chemotherapy in the ER-positive group of patients.

— C Kent Osborne, MD.* Breast Cancer Update *2005, Special CME Meeting Edition

SELECTION OF ADJUVANT CHEMOTHERAPY

For patients with ER-positive disease and multiple positive nodes, I usually use AC with or without a taxane, often dose dense. As we learn more about the biology of these diseases and separate out the cancers by more than just ER-positive and ER-negative, I hope that we can give fewer people chemotherapy.

— Ann H Partridge, MD, MPH.* Patterns of Care *2005 (1)

For adjuvant chemotherapy in the lower-risk, node-negative setting, I generally use four cycles of AC. The controversial issue is whether to use the traditional every three-week schedule or dose-dense therapy with growth factor support. Dose-dense schedules are somewhat better tolerated because of the growth factors, and the patient finishes therapy faster. They come with a great deal of additional cost. Most importantly, however, we probably could benefit from additional validation that AC given every two weeks has an advantage over an every three-week administration. Clearly, dose-dense AC → paclitaxel showed an advantage in CALGB-9741 that most oncologists have accepted. However, whether we can convert that benefit to a lower-risk, node-negative setting with AC times four alone is controversial. In my practice, I discuss with patients the benefits of quicker therapy, the downside in terms of additional injections and cost, and the uncertainty regarding the additional benefit of dose-dense AC. I'm comfortable, however, if a patient chooses to go that route, that we're not doing her any harm.

— Gary H Lyman, MD, MPH.* Patterns of Care *2005 (1)

AC → docetaxel, the control arm in our current US Oncology study, is a very reasonable treatment that doesn't require growth factors. TAC would also be an option. TAC requires growth factors but has about the same treatment duration as dose-dense therapy, and I would use this regimen. We also saw in San Antonio that FEC/docetaxel was significantly better than the standard six cycles of FEC. This is also a legitimate treatment option. In the patient at higher risk, I would pick one of these regimens, and I tend to use AC → docetaxel.

— Stephen E Jones, MD.* Patterns of Care *2005 (1)