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Lymph Nodes in Breast Cancer: So Who's Counting?

ABSTRACT & COMMENTARY

Source: Camp RL, et al. *Cancer* 2000;88:108-113.

Various cytokines may play a role in both local, tumor-induced angiogenesis as well as downstream lymph node genesis and hyperplasia. Camp and colleagues hypothesize that prognostic information might be available by evaluating the downstream effects of malignant tumors. Expression of changes in the lymph nodes could be characterized by either hyperplasia or by an increased number of tumor-free lymph nodes. Because information on the size of lymph nodes is not as readily available, a study was undertaken to evaluate the relationship between the number of uninvolved lymph nodes present and prognosis.

The study included 290 patients with breast cancer whose surgery occurred between July 1, 1983 and July 1, 1993 at Yale-New Haven Hospital. Only node-negative patients with T1-T2 lesions were included. With a median follow-up of 103 months, these early-stage patients had an overall survival of 86.3% and a five-year survival of 93.6%. Treatment was provided by 35 different surgeons, and the specimens were prosected by 77 surgical pathology residents. For this analysis, the tumor size and lymph node number were taken from the original description, but a single pathologist scored the histopathologic features of the primary specimen in a blinded fashion.

The relationship between the number of lymph nodes present and survival in these node-negative patients was examined. With a median follow-up of 103 months, the five-year survival was 84.7% for patients with 20 or more lymph nodes compared with 96.3% if less than 20 nodes were present. In addition to the number of lymph nodes, a univariate analysis also revealed that survival was related to tumor size, grade, and the presence of necrosis. Both tumor size and the presence of 20 or more lymph nodes retained significance in the multivariate analysis. The link between survival and negative nodes may be cytokines which act not only locally to adversely affect the biology of the tumor but also cause downstream lymphogenesis.

INSIDE

COMMENT BY KENNETH W. KOTZ, MD

In this study, a statistical analysis suggested that tumor size (a known factor for survival) was not spuriously associated with the number of lymph nodes removed. For example, larger tumors were not associated with "large" axillary dissections or with an increased number of lymph nodes removed. (Based on recorded dimensions, the cubic volume of the axillary specimen was considered "large" if its size was in the top 25% of all specimens.) Furthermore, the number of lymph nodes removed was not related to either the size of the axillary dissection or the surgeon performing the operation. These results suggest that tumor size did not influence the surgeon to augment the axillary dissection.

Both the level of axillary dissection and the pathologist's preparation of the specimen might affect the results of this study. In this study, a median of 15 lymph nodes were removed, but approximately one-fourth of patients had less than 11 lymph nodes removed. Some of these may have been limited dissections, which is associated with less accurate staging.[1] For a clinically negative axilla, the standard level I-II dissection should include those nodes located lateral to and behind the pectoralis minor and located within the axillary triangle (bordered by the axillary vein superiorly, serratus anterior medially, and the latissimus dorsi laterally).[2] Approximately 18 nodes would be expected from a level I-II dissection [3] although ranges of 0 to 70 have been reported.[2]

The routine technique to identify lymph nodes in the axilla for a pathologic assessment involves a manual dissection.[2,4] The use of fat-clearing fixative, as was used in the majority of cases in this study, increases the number of lymph nodes identified, but has not been associated with significant upstaging.[2,4] Because identifying low numbers of lymph nodes is associated with understaging, my institution performs lymph node enhancement only when less than 10 lymph nodes are found. As can be seen, the pathologist's approach to evaluating the axilla can vary and might change any relationship between lymph node number and survival.

This analysis was restricted to breast cancer patients with T1-T2 tumors whose lymph nodes were negative for malignancy. It would be interesting to test whether the total number of lymph nodes would provide prognostic information for T3-T4 tumors, and compare the level of significance with less advanced tumors. Additionally, I wonder what relationship would emerge between the total number of lymph nodes and prognosis even if some of the lymph nodes contained metastatic deposits. Finally, is this phenonenom restricted to breast cancer? Colon cancer and melanoma are examples of other malignancies where lymph node dissections have been routinely performed and a similar retrospective analysis could be undertaken. Of course, the increasing use of sentinel lymph node biopsies may make unavailable any real prognostic information that the total number of lymph nodes provides.

So who's counting? If, as the title of this article suggests, "a high number of tumor-free axillary lymph nodes from patients with lymph node negative breast carcinoma is associated with a poor outcome," we may be counting lymph nodes, even when node-negative. ❖

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Prostate-Specific Membrane Antigen Levels in Sera as a Possible Biomarker for Prostate Cancer

ABSTRACT & COMMENTARY

Synopsis: *Prostate-specific membrane antigen (PSMA) was evaluated as a potential biomarker for the diagnosis and monitoring of patients with prostate cancer. While serum measurements of PSMA could be reliably made by Western blot analysis, this measurement was not shown to be a specific biomarker for prostate cancer.*

Source: Beckett ML, et al. *Clin Cancer Res* 1999;5: 4034-4040.

Prostate cancer remains an extremely common disease. Projections for the year 2000 are that 180,400 new cases of prostate cancer will be diagnosed in American men. In addition, 31,900 American men are anticipated to die due to prostate cancer in the year 2000. These figures will make prostate cancer the leading cause of new cancers and the second leading cause of cancer deaths in American men for the year 2000 (the figures exclude basal and squamous cell skin cancers and in situ carcinomas).[1] Thus, prostate cancer is a major health concern for American men.

Measurements of prostate-specific antigen (PSA) have been used for the diagnosis and monitoring of patients with prostate cancer.[2-4] Current American Cancer Society recommendations include offering the PSA blood test and digital rectal exam (DRE) on an annual basis, beginning at age 50, to men who have at least a 10-year life expectancy and to younger men at high risk.[5] However, no prospective, randomized study of PSA screening has been completed which uses prostate cancer-specific mortality as its endpoint. Thus, controversy remains regarding use of PSA as a routine screening test. Since PSA is prostate-specific but not cancer-specific, several non-malignant conditions of the prostate can cause an elevation of PSA values. These conditions include benign prostatic hypertrophy (BPH), as well as prostatitis, and physical exam manipulation of the prostate gland. Thus, it would be desirable to have a biomarker which could differentiate abnormalities of serum PSA due to benign conditions vs. elevations of serum PSA due to prostate cancer.

Several refinements have been proposed to improve the positive predictive value of elevated PSA for the identification of prostate cancer. These strategies include the use of age-specific reference ranges for serum PSA, as well as the use of a PSA density value. The PSA density refers to a quotient of serum PSA and prostate volume.[6] Another strategy is to use serial measurements of PSA to identify a yearly rate of change in PSA values. This value, termed "PSA velocity," can also increase the positive predictive value of PSA measurements for prostate cancer.[4,7] In addition, measurements of PSA can be obtained to identify free PSA vs. complexed PSA vs. total PSA. The percentage of free PSA is lower in serum samples from patients with prostate cancer than in serum samples from patients with non-malignant prostate conditions.[8] Thus, measurements of free/total PSA values have been proposed as a useful measurement in patients with borderline elevations of PSA.

Prostate-specific membrane antigen (PSMA) is a transmembrane lipoprotein in prostate epithelial cells which has been proposed as a possible biomarker for patients with prostate cancer. Beckett et al used electrophoresis and Western blotting to measure PSMA levels in the sera of 236 normal individuals and cancer patients. Beckett and colleagues confirmed reproducible measurements of serum PSMA by Western blot analysis. Levels of PSMA were shown to be significantly elevated in men older than 50 years of age when compared with samples from younger men. However, measurement of serum PSMA was unable to distinguish early-stage prostate cancer from BPH, and measurement of PSMA was not more effective than PSA in monitoring prostate cancer patients. Beckett et al conclude that PSMA is not a specific biomarker for prostate cancer.

COMMENT BY MARK R. ALBERTINI, MD

The study reported by Beckett et al demonstrates a technique for measurement of serum PSMA in the sera of normal individuals and cancer patients. Values for PSMA were shown to increase with age, as serum values for men older than 50 years of age were greater than serum values of men younger than 50 years of age. Conditions such as benign prostatic hypertrophy and prostatitis did not increase values above age-adjusted comparison values. Values for patients with early stage (T1 and T2) prostate cancer were lower than those with a similar age control group, while patients with late-stage (T3) prostate cancer had a trend to an increased value over a similar age control group. However, values for patients with stages T2 and T3 disease were higher posttreatment (mean PSMA integrated intensity units: 6.06) than were values for a similar group of patients with T2 and T3 disease pretreatment (mean PSMA value of 3.09). The PSMA values for individual prostate cancer patients receiving treatment added no additional informa-

tion above that available by measurement of PSA.

Sera from normal women and from breast cancer patients were also evaluated and shown to have detectable levels of PSMA. The source of PSMA in non-prostate tissues, including samples from women, remains unclear. Thus, the current assay for PSMA does not provide a specific biomarker for patients with prostate cancer. While further refinements of this assay may prove useful, additional evaluation with a larger number of patients in each diagnostic category will be required to evaluate its role for prostate cancer patients. ❖

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Early Initiation of Adjuvant Chemotherapy for Premenopausal Breast Cancer

ABSTRACT & COMMENTARY

Synopsis: *It appears that there is a survival advantage for premenopausal patients who have ER-negative tumors if they were treated within 21 days of initial surgery, compared to those in whom adjuvant chemotherapy was started later (i.e., after 21 days).*

Source: Colleoni M, et al. *J Clin Oncol* 2000;18:584.

The initiation of adjuvant breast cancer chemotherapy varies for a number of factors and it had not been clearly demonstrated that earlier treatment is beneficial. This question was addressed by the International (Ludwig) Breast Cancer Study Group (IBCSG). Using data from trial V at a median follow-up of 11 years, there was a suggestion that earlier treatment was associated with better outcomes. Thus, a larger analysis was undertaken.

The experience of node-positive, premenopausal patients (n = 1788) treated on IBCSG trials I, II, and VI was examined to address the relationship between early initiation of adjuvant chemotherapy, estrogen receptor (ER) status, and prognosis. The disease-free survival for 599 patients (84 ER-negative) who commenced adjuvant chemotherapy within 20 days (early initiation) was compared with the disease-free survival for the remainder of the group (1189 patients, 142 of which were ER-negative) who started their chemotherapy 21 to 86 days after surgery (conventional initiation). The median follow-up was 7.7 years.

Among those with ER-negative tumors, the 10-year disease-free survival was 60% for the early initiation group compared with 34% for the conventional initiation group. This difference was statistically significant and remained so after multiple regression analysis which factored out the influence of number of positive nodes, tumor size, patient age, vessel invasion, or treating center. Conversely, early initiation of chemotherapy did not significantly improve disease-free survival for patients with ER-positive tumors.

COMMENT BY WILLIAM B. ERSHLER, MD

Although it makes sense that early therapy is prudent, published experience from large trials has been inconclusive. There have been a few trials that would suggest that early intervention with adjuvant chemotherapy was beneficial.[1,2] The experience from the National Surgical Adjuvant Breast and Bowel Project (NSABP), particularly Trial B-18, would seem to be in conflict. However, the current examination revealed a survival benefit only for a distinct subgroup, those premenopausal patients who were ER-negative. The NSABP trial, which demonstrated comparable survival for patients who received preoperative or postoperative chemotherapy, did not report the data in terms of ER status.[3]

Perioperative chemotherapy has been shown to benefit some subgroups of patients, and it might be these same subgroups that would benefit from early adjuvant therapy. A recent meta-analysis of published reports on perioperative chemotherapy indicated that this approach reduced the risk of relapse by 17% for women less than 50 years of age.[4] Here too, the ER status was not reported. Yet, there has been at least one study that showed that the subgroup most positively influenced by perioperative therapy was the ER-negative group.[5]

A theoretical rationale for early intervention can be derived from animal models in which surgical excision

of primary tumors results in an increased growth fraction and angiogenesis in metastatic lesions.[5,6] Thus, shortly after surgery, metastatic cells might be more susceptible to cycle-specific chemotherapy or even anti-angiogenic agents.

This was a retrospective examination and all the caveats regarding overinterpretation of such are in effect. Nonetheless, the finding of enhanced survival in those ER-negative, premenopausal, early-treated patients was quite robust, and the analysis was appropriately balanced with regard to other prognostic factors. The conclusion that early adjuvant therapy is likely to benefit this group is probably correct, but a prospective study would likely settle the issue. ❖

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Patient Education by Computer

ABSTRACTS & COMMENTARY

Synopsis: *Patients are increasingly obtaining medical information from computer-based sources and, these days, physicians are commonly handed print-outs that may or may not be relevant to the patient's medical condition. In two reports from the Department of Public Health at the University of Glasgow, research is presented that indicates that as many as 20% of cancer patients about to begin a course of radiation therapy are dissatisfied with the information they have been provided about their illness or treatment.*

Sources: Jones R, et al. *BMJ* 1999;319:1241-1247; Jones R, et al. *BMJ* 1999;319:1247-1248.

Computers are in the mainstream and patients are increasingly using the internet to gain information relevant to their own medical condition. In companion articles written by faculty from the department of Public Health at the University of Glasgow, Scotland, patient education and computer use was examined.

The purpose of the first report was to compare the use and effect of a computer-based information system that is personalized to an individual patient's medical record with a system providing only general information, either by computer or by written booklets. Volunteers were patients (n = 525) about to begin a course of radiation therapy. They were randomly assigned to one of three groups: computer personalized information, computerized general information, and general information by booklet. Patients' views and preferences, use of computer and information, and psychological status were the measured outcomes as well as doctors' perceptions and costs.

As expected, more patients offered the personalized information said that they had learned something new, thought the information was relevant, used the computer again, and showed their computer printouts to others. There were no major differences in doctors' perceptions of patients. More of the general computer users were anxious at three months. Cost analysis showed that the computer information systems were less expensive over time than full use of booklet education.

The second report describes a cross sectional survey of these same 525 cancer patients, most of whom had breast cancer (n = 309) and were about to receive radiation therapy. Data from a recruitment interview, subsequent questionnaire, and from their clinical notes were examined, with a goal of determining their satisfaction with the medical information that had been provided to them up until that point. Four of five patients wanted as much information as possible and one in five were not satisfied with the information they had been provided. Dissatisfied patients were much more likely to be depressed and anxious.

COMMENT BY WILLIAM B. ERSHLER, MD

Although it is apparent that computer use among oncology patients is rising dramatically, the concept of personalizing educational programs is not developed. Experiments have been published in which different ways of personalizing computer-based information for patients is assessed, a study comparing this approach with general computer-based information retrieval has not previously been published.

The current trial showed that cancer patients thought a system giving them information based on their medical records was better than one giving only general information and they were more likely to use it repeatedly and show printouts to their family and doctors. The doctors were not able to perceive a difference in patients from the different groups, but patients assigned to the general computer information group were more likely to be anxious at the three months follow-up.

Although not specifically addressed in this report, physician's acknowledgment of the computer-based education might be higher with the personalized pro-

gram as well. Most clinicians are inundated with printouts from patients, and much of the provided material seems unrelated or only remotely related to the patient's condition. The specialty of medical informatics is in its infancy and it should be expected that, within the next decade, highly sophisticated software will be developed that will provide a high level of specific information to our patients. It is also likely that cancer patients will be among the first to take advantage of this emerging technology. ❖

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Treatment of Relapsing or Recalcitrant Cutaneous T-Cell Lymphoma with Pegylated Liposomal Doxorubicin

ABSTRACT & COMMENTARY

Synopsis: *Six patients with biopsy-proven, relapsing or recalcitrant mycosis fungoides were treated with pegylated liposomal doxorubicin (20 mg/m^2) monthly. The response rate was 83% with four patients achieving a complete response. Toxicity was minimal.*

Source: Wollina U, et al. *J Am Acad Dermatol* 2000; 42:40-46.

This prospective study enrolled six patients ages 59-78 with mycosis fungoides and adequate hematologic, hepatic, and renal function. All patients had either T2N0M0 (stage Ib) or T3N0M0 (stage IIb) disease. A complete response required the absence of detectable residual disease as determined by a follow-up skin biopsy, irrespective of the presence of post-inflammatory hyperpigmentation. A partial response required either a greater than 50% decrease in the size of lesions or a reduction in more than half of the nodular and plaque-like lesions into macules.

Treatment consisted of a maximum of eight cycles of pegylated liposomal doxorubicin given at a dose of 20 mg/m^2 monthly. For these patients with an excellent performance status (Karnovsky index 90% or higher), the toxicity was minimal. Furthermore, the patients were not heavily pretreated. Although all patients had been exposed to either extracorporeal photochemotherapy, PUVA, or selective UV broad-spectrum phototherapy, only one patient had previously received cytotoxic chemotherapy. Four patients had received alpha interferon during extracorporeal photochemotherapy. Although the eligibility criteria were for patients with "recalcitrant" and "relapsing" disease, the patients did not seem particularly refractory with the prior response consisting of either a complete response (1 patient), a partial response (3 patients), or progressive disease (2 patients).

Four patients achieved a complete response documented histologically with a post-treatment punch biopsy. One patient had a partial response and there was one with progressive disease. The time to best response ranged from two to eight cycles.

COMMENT BY KENNETH W. KOTZ, MD

Mycosis fungoides, as described in the R.E.A.L. classification, is a T-cell non-Hodgkin's lymphoma characterized by multiple cutaneous plaques or nodules.[1] Mycosis fungoides is not considered synonymous with cutaneous T-cell lymphoma (CTCL) by all authors, as the latter term may also include other non-Hodgkin's lymphomas that involve the skin, such as peripheral T-cell lymphoma and adult T-cell leukemia/lymphoma.[1,2]

In this study, an impressive response rate, including four of six patients with a pathologic complete response, was seen. However, these patients were not heavily pretreated and some were not refractory to previous therapy. Options available for patients with mycosis fungoides include topical chemotherapy, PUVA, photophoresis (extracorporal photochemotherapy), total skin electron beam radiation, interferon, and a variety of systemic, cytotoxic chemotherapy agents.[2] Monoclonal antibodies such as the anti-CD52 CAMPATH-1H have shown responses in mycosis fungoides.[3] Activity has also been demonstrated with retinoids including targretin (bexarotene), a high-affinity ligand for the retinoid X-receptor, which was just approved by the FDA.[2,4] Finally, a unique approach for CD25-expressing (the IL-2 receptor) CTCLs has been achieved with ONTAK (denileukin diftitox), a combination protein containing diptheria toxin and interleukin-2.[2,5]

In the title of the article, Wollina and colleagues state "pegylated liposomal doxorubicin" was the product they studied. Caelyx was the brand of encapsulated doxorubicin they used, which is called doxil in the United States. Pegylation is a process by which polyethylene glycol, a hydrophobic polymer, is linked to proteins. This modification results in a pharmaceutical that tends

to have a longer half-life and less antigenicity while retaining its biologic activity. For example, oncologists are familiar with oncaspar (pegaspargase), a pegylated form of asparaginase for acute lymphocytic leukemia with an improved therapeutic index over asparaginase. Liposomes are nontoxic, biodegradable, lipid particles which deliver the encapsulated drug compounds to target tissues with less toxicity than the native compound. Examples would include several liposomal amphotericin B preparations which are less toxic than standard amphotericin B, and daunoxome, a liposomal preparation of daunorubicin.

Doxil contains doxorubicin in a carrier system using "STEALTH" liposomes which are formulated with a form of polyethylene glycol, hence, the term "pegylated, liposomal doxorubicin."[6] This form of pegylation appears to protect the liposomes from the mononuclear phagocyte system and increase blood circulation time.[6] In the United States, doxil is approved for the treatment of ovarian cancer (50 mg/m^2 every 4 weeks) and AIDS-related Kaposi's sarcoma (20 mg/m^2 every 3 weeks). In this preliminary study by Wollina et al, a schedule of 20 mg/m^2 every month appeared to have potential activity in the early stages of mycosis fungoides. ❖

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Evaluation of Temozolomide for Patients With Advanced Metastatic Melanoma

ABSTRACT & COMMENTARY

Synopsis: *Temozolomide and DTIC had similar efficacy in this prospective, randomized study. However, overall treatment results for this patient population remain dismal and discovery of new treatment approaches for patients with metastatic melanoma is greatly needed.*

Source: Middleton MR, et al. *J Clin Oncol* 2000;18: 158-166.

The success of various chemotherapy strategies for patients with metastatic melanoma has been limited. The use of single-agent dacarbazine (DTIC) has been a "standard" treatment, but the modest response rate of 15-20%, with most of the responses being of brief duration, certainly leaves ample room for improvement.[1] A recent study from the Eastern Cooperative Oncology Group (ECOG) randomized 258 eligible patients with metastatic melanoma to receive treatment with dacarbazine either alone or combined with tamoxifen, interferon-alpha, or both tamoxifen and interferon-alpha. There was no difference between time-to-treatment failure (median of 2.6 months) or overall survival (median of 8.9 months) between any of the four treatment groups.[2] Thus, neither tamoxifen, interferon-alpha, nor the combination of tamoxifen and interferon-alpha were able to improve response rate, time-to-treatment failure, or survival of melanoma patients when these treatments were added to single-agent therapy with dacarbazine. Several additional chemotherapy regimens have been evaluated for patients with metastatic melanoma, but results from these studies have not yet identified a chemotherapy regimen that is clearly better than single-agent dacarbazine. Thus, discovery of new drugs with clinical activity against melanoma is greatly needed.

Temozolomide, like DTIC, is a pro-drug of the active alkylating agent 5-(3-methyltriazen-1yl)imidazole-4-carboximide (MTIC). However, temozolomide, unlike DTIC, is active following oral administration.[3] In addition, temozolomide can penetrate the blood-brain barrier and has shown activity against primary brain tumors.[4] Initial phase II evaluation of temozolomide in metastatic melanoma revealed an objective response rate of 21% and a median survival time of 5.5 months.[5] Thus, the study by Middleton and colleagues was initiated to compare overall survival of patients with advanced melanoma treated with either temozolomide or DTIC and to compare the safety of these treatments. Middleton et al conclude that temozolomide has efficacy equal to that of DTIC and provides an oral alternative for patients with advanced metastatic melanoma.

COMMENT BY MARK R. ALBERTINI, MD

Malignant melanoma remains an increasingly common disease. Recent estimates from the American Cancer Society are that there will be 47,700 new cases of melanoma in the United States in the year 2000.[6] Since 7700 deaths due to melanoma are expected to occur this year, this is an important clinical problem. Many of these patients will be young, as the average age at diagnosis of patients with melanoma is approximately 50 years.[7] While early melanoma can be a cur-

able disease, the successful treatment of patients with metastatic disease remains elusive. The average survival for patients with metastatic melanoma is about seven months, and the percentage of patients with metastatic melanoma alive at five years is approximately 6%.[8] Thus, further improvements in our treatment are critically needed.

The study by Middleton et al demonstrates the comparable activity of temozolomide and DTIC for patients with advanced metastatic melanoma and no CNS involvement. Overall survival and objective response rates were similar in the two treatment groups. Middleton et al describe a significant increase in progression-free survival (PFS) in patients treated with temozolomide (1.9 months) compared with patients treated with DTIC (1.5 months). However, this minimal increase could easily be explained by the difference in timing of disease status assessment for patients, as the DTIC treated patients had assessment for disease progression two weeks earlier than did the temozolomide treated patients. Overall, safety parameters of the treatments were similar, and a slight benefit in quality-of-life parameters assessed by a questionnaire at week 12 was present in the temozolomide group. Thus, the current study supports comparable activity of temozolomide and DTIC for patients with metastatic melanoma. However, overall results for both treatment groups remain poor.

Several nonrandomized, single institution, phase II studies have evaluated Interleukin-2 (IL-2) given together with interferon-alpha and combination chemotherapy for patients with metastatic melanoma. These biochemotherapy regimens have included both inpatient and outpatient regimens, and response rates of 40-60% have been reported.[9-11] In addition, up to 10% of these patients have achieved a durable complete response. An intergroup, phase 3, randomized study is now ongoing to compare chemotherapy with dacarbazine, cisplatin, and vinblastine either alone or in combination with IL-2, Interferon-a2b, and G-CSF for patients with metastatic melanoma. The aim of that study is to determine whether immunotherapy adds additional benefit to a chemotherapy regimen for patients with metastatic melanoma.

There remains no standard treatment for patients with metastatic melanoma. Various options including no treatment, surgery, radiation therapy, chemotherapy, immunotherapy, biochemotherapy, and an increasing number of experimental options may be appropriate considerations for an individual patient. Given the limited results from "standard" treatments, participation in a well-designed clinical trial remains a valuable option for patients with this disease. ❖

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CME Questions

10. From the study by Camp et al on the relationship between lymph node number and survival in breast cancer, which of the following is true?

a. Larger axillary dissections contained an increased number of lymph nodes.
b. Patients were randomized to different levels of axillary lymph node dissection.
c. Patients with the most aggressive axillary lymph node dissections had the best survival.
d. Patients with less than 20 lymph nodes survived longer than patients with more than 20 lymph nodes.

11. Which one of the following statements about PSMA is true?

a. PSMA has been shown to be a specific biomarker for prostate cancer.
b. PSMA can be detected in serum samples from a healthy female population.
c. PSMA values are higher in serum samples from men younger than 50 years of age compared with serum samples from men older than 50 years of age.
d. Conditions such as benign prostatic hypertrophy and prostatitis have been shown to increase PSMA values above age-adjusted comparison values.

In Future Issues:

Overexpression of Her-2 in Unknown Primary Carcinomas