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Limited Lung Resection and Brachytherapy May Benefit Cancer Patients Whose Lung Function is Compromised

ABSTRACT & COMMENTARY

Synopsis: *The standard of care for early lung cancer is surgery. However, in aged or frail patients, or in those whose pulmonary or cardiac status is compromised, radical surgery may be contraindicated. Alternatives are observation, external beam radiotherapy, and limited resection in conjunction with brachytherapy. The latter has the advantage of selectively irradiating the regions at highest risk for local recurrence, while sparing the adjacent normal lung. Investigators from Tufts University reported results in a series of 33 patients who were followed for a minimum of 20 months and concluded that brachytherapy might improve the outcome following limited resection for early lung cancer.*

Source: Lee W, et al. *Ann Thorac Surg*. 2003;75:237-243.

Between 1993 and 2000, Lee and colleagues at the Tufts New England Medical Center performed implants of I-125 seeds arranged in suture strands after limited resection of early stage non-small-cell lung cancers in 33 medically compromised patients. These patients were not lobectomy candidates because of poor pulmonary function (n = 21), poor cardiac status (n = 6), or age older than 75 years with refusal to undergo lobectomy (n = 6). All patients had an FEV_1 of < 1.0 liters or were intolerant of < 1 flight of stairs. Median patient age was 69 years (age range, 46-86). There were 35 resections, including 32 wedge resections and 2 segmental resections. All patients were staged preoperatively with CT scans, and intraoperatively, 19 underwent mediastinal nodal sampling/dissection while 3 had mediastinoscopy. There were 19 patients with T1N0 disease (58%), 10 with T2N0 disease (30%), and 1 each with T2N1, T1N2, T3N0, and unspecified disease. Lee et al performed a retrospective analysis in order to determine whether I-125 brachytherapy was effective at reducing lung cancer recurrences at the surgical margin.

Each limb of the wedge resection was approximately 6 cm in

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length. Gross surgical margins were > 1 cm. One to 3 I-125 strands with 10 seeds apiece were implanted at or near both sides of the resection margin. The prescribed dose was 125-140 Gy at 1-cm depth. The I-125 strands were secured in place with 3-0 silk sutures. The average strength per seed was 0.7 mCi.

Minimum follow-up in all patients was 20 months. There were no complications related to brachytherapy. There was 1 operative death related to ARDS. Implant quality was assessed via orthogonal x-rays or CT-based 3D reconstruction. Patients were assessed clinically with a chest x-ray during the follow-up period. Local recurrence was defined as failure at the resection margin, and regional recurrence was a failure at either the mediastinum, chest wall, or ipsilateral lung. The overall recurrence rate for the entire group was 30%, including 5 locoregional recurrences (15%), 2 distant recurrences (6%), and 3 with both (9%). Among T1N0 patients, 36% developed locoregional recurrences, including 2 with local recurrences (10.5%) and 5 (26%) with regional failures. There were 4 other regional recurrences (12%). Median overall survival for the entire group was 45 months. The projected 5-year disease-free survival (DSF) for T1N0 patients was 77%, and it was 53% for the T2N0 patients. For the whole group, the projected 5-year DFS rate was 61%.

Lee et al concluded that their results were comparable to those in the literature and that limited resection accompanied by brachytherapy is a reasonable compromise in patients who are not suitable for lobectomy. Compared to nonoperative management (ie, external beam radiotherapy) there is more lung sparing. Longer follow-up is needed to validate whether brachytherapy indeed reduces the incidence of local recurrence following wedge resection for early lung cancer.

COMMENT BY EDWARD J. KAPLAN, MD

Wedge lung resections are known to be plagued by local recurrences, as reported by the Lung Cancer Study Group in their published randomized trial results[1] cited by Lee et al in the above study. In general, survival following lobectomy was cited by Lee et al as being in the 40-75% range and 13-21% following definitive radiotherapy. The latter range seems somewhat low for modern RT series. For example, data from M.D. Anderson Cancer Center included 3-year local control rates of 89% and 61% for medically inoperable T1 and T2 patients, respectively, and DFS rates of 49% and 47% with doses > 60 Gy.[2] Sibley and associates from Duke University published an overview of 10 studies where primary RT was used to treat medically inoperable stage I NSCLC patients and reported that 30% of patients die of distant metastases, while another 30% die due to local failure. Trials of dose escalation were suggested.[3]

Interestingly, the Japanese have conducted retrospective analyses of 2 different forms of dose escalation. Uematsu et al treated 50 patients from 1994-1999 with CT-guided frameless stereotactic radiotherapy delivering 50-60 Gy in 5-10 fractions with or without supplemental conventional RT and reported a 3-year DFS of 88%.[4] Fukumoto et al used small-volume hypofractionated image-guided RT to deliver 48 or 60 Gy in 8 fractions to patients with stage I tumors. They reported a 67% 2-year DFS rate at 24 months follow-up.[5] Based on such studies, dose escalation to limited lung volumes does appear to offer a benefit. Therefore, although using radioactive seeds in sutures is not a new idea,[6-7] it may offer a timely, convenient, and effective way of sterilizing the surgical margin in the setting of minimally invasive surgery, as in wedge resections that might be done thoracoscopically. ■

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Capecitabine with Gemcitabine for Advanced Pancreatic Cancer: Results from a Swiss Phase I/II Trial

ABSTRACT & COMMENTARY

Synopsis: *Although gemcitabine has been proven to be of value in the treatment of advanced pancreatic cancer, remission rates remain low and survival is measured in weeks to months. Swiss investigators report the results from a phase I/II study of combined gemcitabine/capecitabine treatment. The trial resulted in a recommended dose and schedule for the combination and some optimism that the drugs will be shown to work synergistically for patients with advanced pancreatic cancer.*

Source: Hess V, et al. *J Clin Oncol*. 2003;21:66-68.

THERE ARE PRECLINICAL STUDIES THAT SUGGEST THAT the addition of capecitabine to the current standard treatment for advanced pancreatic cancer (gemcitabine) would offer additional value with little risk. To test this clinically, Hess and collaborators from Switzerland performed a phase I/II trial in patients with advanced pancreatic cancer (APC).

Thirty-six chemotherapy-naïve patients with nonresectable or metastatic pancreatic carcinoma were treated with gemcitabine at a fixed dose of 1000 mg/m^2 on days 1 and 8 of a 21-day cycle. Capecitabine was given in increasing doses orally b.i.d. for 14 days, followed by a 1-week rest. Dose-limiting toxicity (DLT) occurred at a dose of 800 mg/m^2 of capecitabine and consisted of myelotoxicity and mucositis. Hand-foot syndrome was not observed, and other toxic effects were mild. Thus, Hess et al recommend a dose of capecitabine of 650 mg/m^2 when used with gemcitabine at 1000 mg/m^2 on days 1 and 8 of a 21-day cycle.

With regard to observed responses, in the 27 patients with measurable disease, there were 1 complete and 4 partial remissions. In addition, significant drops (> 50% from baseline value) of the tumor marker CA 19-9 occurred in 14 of the 24 assessable patients.

COMMENT BY WILLIAM B. ERSHLER, MD

The current standard regimen for patients with advanced pancreatic cancer is single-agent gemcitabine.[1] Although the addition of infusional 5-flurouracil has not been shown to increase treatment efficacy,[2,3] the potential role for capecitabine in combination with gemcitabine had not been previously reported specifically for pancreatic cancer patients.

This phase I/II report offers a reasonable dose and schedule for the much-needed phase III study, currently underway, in which the combination is compared to gemcitabine monotherapy. The suggested dose of capecitabine (650 mg/m^2) is somewhat lower than has been reported in a larger phase I study that included pretreated patients with various types of tumors.[4] In that report, capecitabine at 830 mg/m^2 given b.i.d. for 21 days with gemcitabine at 1000 mg/m^2 weekly on days 1, 8, and 15 of a 28-day cycle, was considered tolerable. Hess et al suggest that the lower acceptable dose might be an indication of an increased susceptibility to toxicity in patients with pancreatic cancer.

Although this is a phase I/II report with a primary goal of determining toxicity and recommended dose and schedule, there is some room for optimism that the combination will be better than gemcitabine given alone when subjected to a clinical trial. Of the 24 patients who had elevated CA19-9 prior to treatment, 14 had a more than 50% reduction with treatment. Such a reduction has been shown by others[5] to be associated with increased survival, even in the absence of achieving imaging criteria for remission.

Pancreatic cancer is among the most resistant of all tumors encountered, and clinicians are constantly frustrated by the lack of effective treatment options. Thus, this preliminary report offers some room for cautious optimism that these 2 drugs will work synergistically in providing more quality time for patients with advanced pancreatic cancer. Small steps for little feet. ■

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Tamoxifen Alone vs Adjuvant Tamoxifen for Operable Breast Cancer in the Elderly

ABSTRACT & COMMENTARY

Synopsis: *Breast cancer is the most common malignancy in women and is very common in older patient populations. Women older than age 70 comprise 15-20% of patients. Some of these older patients may not be able to tolerate or do not desire the standard surgical procedures of either lumpectomy or mastectomy. In addition, as these patients will be an increasing proportion of the overall breast cancer population, it is important to define which aspects of treatment are most critical to overall outcome. This is helpful to the individual patients and their families so they can make an informed choice. It is also critically important to physicians and health care planners. Two randomized trials showed no difference in survival between elderly patients treated with tamoxifen alone or surgery alone. One study showed that locoregional control was better in the surgery group, but the differences were not statistically significant. Another trial reported a high rate of local relapse after surgery.*

Source: Mustacchi G, et al. *Ann Oncol.* 2003;14: 414-420.

This paper presents the long-term results of the Italian Trial, GRETA, after analysis of local responses, distant metastases incidence and dates, and causes of death. This was a randomized, multicenter phase III study that compared the efficacy of tamoxifen alone vs surgery followed by adjuvant tamoxifen in women older than 70. Eligibility required histologic evidence of invasive breast cancer that was potentially operable. Patients were randomized to tamoxifen alone (160 mg loading dose day 1, followed by 20 mg daily) for 5 years or surgery followed by tamoxifen 20 mg/d for 5 years. The extent of surgery was not prescribed and radiation therapy was not part of the study. Between March 1987 and June 1992, 474 women older than 70 with operable breast cancer were recruited. The median age of the patients was 76 years, and the majority of the tumors were T1 (55.2%), with 60.3% of patients N0.

In the tamoxifen-alone group, there was 41.6% response rate (CR+PR). At a median follow-up of 80 months, 11.2% of patients in the surgical arm and 45.2% in the tamoxifen-alone arm had a local progression. No difference in breast cancer deaths was found between the 2 groups of treatment. Deaths from other causes were highly significant. Fifty percent of patients without recurrence died from cardiovascular disease. This has been seen in trials of lymphoma and prostate cancer in elderly patients.[1,2]

The role of tamoxifen in the adjuvant treatment of postmenopausal women is well established.[3] The current study demonstrated that local therapy did not influence survival, as there was no difference between the 2 arms. However the high rate of local progression in the tamoxifen-alone group indicates that minimal surgery followed by adjuvant tamoxifen is the most appropriate treatment in older patients with operable breast cancer. Tamoxifen alone is an alternative as sole first-line treatment only in frail patients unfit for surgery or refusal. The loading dose used in the surgery arm of the trial may have led to the longer distant metastases-free survival in favor of the tamoxifen-alone group.

COMMENT BY STUART M. LICHTMAN, MD, FACP

This study adds more information to the treatment algorithm of breast cancer in elderly patients. It also confirms earlier data that in clinical trials in elderly patients, overall survival is often influenced by other factors, particularly comorbidity. If one is looking at overall survival and is not concerned about locoregional recurrence, tamoxifen alone, in an estrogen receptor positive tumor, may be an appropriate alternative. In an attempt to define breast cancer therapy in elderly women, it has been shown that radiation therapy may be withheld without a significant effect on survival.[4] This again indicates that local therapy does not significantly influence overall survival. This study has some limitations. It does not address the issue of adjuvant radiation therapy. It also did not specify the type of surgery the patients were to receive or the need for axillary dissection. It is also not possible to know whether the use of aromatase inhibitors would give the same results. Patients should be made aware of their treatment options and what role each modality plays in local recurrence, systemic recurrence, and overall survival.

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Toward Developing a Rational Strategy for Advanced Lung Cancer Treatment in the Elderly

ABSTRACT & COMMENTARY

Synopsis: *In a multicenter, Italian, randomized, phase III trial, single-agent vinorelbine or gemcitabine proved to be as effective as a combination of the 2 agents in the treatment of advanced non-small-cell lung cancer occurring in patients 70 years and older. For the most part, toxicity was less with single-agent therapy (vinorelbine or gemcitabine) compared with the combination, but indicators of quality of life were comparable in all 3 treatment arms.*

Source: Gridelli C, et al. *J Natl Cancer Inst*. 2003;95: 362-372.

Lung cancer occurs commonly in elderly patients, many of whom have significant comorbidities that might preclude effective antineoplastic therapy. Yet in a prior study,[1] this Italian group demonstrated that elderly patients treated with single-agent vinorelbine had improved overall survival (median of 28 vs 21 weeks) and scored better on certain measures of quality of life, when compared to patients who were treated with supportive care alone (without antineoplastic drug). In the current study, the combination of vinorelbine plus gemcitabine was compared to either agent administered alone in elderly patients with advanced lung cancer.

Patients aged 70 years and older were randomly assigned to receive intravenous vinorelbine (30 mg/m^2), gemcitabine (1200 mg/m^2), or vinorelbine (25 mg/m^2) plus gemcitabine (1000 mg/m^2). All treatments were delivered on days 1 and 8 every 3 weeks for a maximum of 6 cycles. The primary end point was survival and secondary outcomes were quality of life and toxicity.

Of 698 patients available for intention-to-treat analysis, 233 were assigned to receive vinorelbine, 233 to gemcitabine, and 232 to vinorelbine plus gemcitabine. Compared with each single drug, the combination treatment did not improve survival. The hazard ratio of death for patients receiving the combination treatment was 1.17 (95% confidence interval [CI], 0.95-1.44) that of patients receiving vinorelbine, and 1.06 (95% CI, 0.86-1.29) that of patients receiving the gemcitabine. Although quality of life was similar across the 3 treatment arms, the combination treatment was more toxic than the 2 drugs given singly.

Gridelli and associates concluded that the combination of vinorelbine plus gemcitabine is not more effective than single-agent vinorelbine or gemcitabine in the treatment of advanced non-small-cell lung cancer in elderly patients.

COMMENT BY WILLIAM B. ERSHLER, MD

The median age of newly diagnosed lung cancer is approximately 68 years, and as many as 40% may be older than 70 years at diagnosis.[2] For younger adults with advanced disease, cisplatin-based chemotherapy regimens have become standard management,[3] but there has long been concern that older patients, particularly those with significant comorbidities, would experience unacceptable toxicities with these aggressive regimens. Thus, until recently, it was common practice to exclude older lung cancer patients from chemotherapeutic intervention.

In 1999, the Elderly Lung Cancer Vinorelbine Italian Study (ELVIS) was published demonstrating that single-agent vinorelbine was superior to best supportive care in both survival and quality of life. The MILES study was designed to test the hypothesis that the combination of vinorelbine with gemcitabine would be better than either agent alone. The rationale for this conjecture was that drugs have been shown to be active in non-small-cell cancer, both are well tolerated by older patients,[1,4] and each has a distinct mechanism of action. However, the results did not show benefit for the combination in terms of survival, and, although quality of life was similar across all 3 treatment arms, the combination treatment was more toxic that the 2 drugs given singly. The study wasn't designed to compare vinorelbine and gemcitabine as single agents, but it appears that they are comparable with regard to efficacy and toxicity. Future studies, no doubt, will compare other agents, such as the taxanes, or Iressa, either alone or in combination. However, until new data are available, single-agent vinorelbine or gemcitabine may well be considered standard of care for elderly patients with advanced non-small-cell lung cancer.

The Italian investigators who brought us ELVIS and now MILES should be commended for their groundbreaking work in geriatric oncology. These studies incorporated many of the factors determined to be relevant in geriatric medicine, including a pretreatment geriatric assessment and outcomes that included a determination of quality of life. There is now an increasing awareness that close to 50% of cancer occurs in patients older than age 65. Trials that focus on management in typical patients who are likely to have comorbidities and various functional impairments will be of increasing importance in the decades to come. ■

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Increased Risk of Breast Cancer with Estrogen-Progestin Therapy

ABSTRACT & COMMENTARY

Synopsis: *Postmenopausal estrogen-progestin therapy increased the risk of breast cancer in a population-based cohort in Sweden, and estrogen-only did not.*

Source: Olsson HL, et al. San Antonio Breast Cancer Symposium, December 2002. Abstract 34. In press.

OLSSON AND COLLEAGUES FROM LUND SWEDEN reported about 2 years ago[1] the incidence of breast cancer in a population-based cohort of 29,508 women. The women were recruited between 1990-1992, and followed for a median time of 7.6 years. There were 434 cases of breast cancer compared with 388 cases expected according to national statistics, which amounted to an increased risk of 1.92 with 4-10 years of postmenopausal estrogen-progestin use. There was no interaction with family history of breast cancer among first-degree relatives or previous use of oral contraceptives. That report was recently updated at the San Antonio Breast Cancer Symposium in December 2002. The number of breast cancers now totals 556 vs 508 expected. This produced a calculated overall increased risk of 1.09 that almost but not quite reached statistical significance. The risk for users of combined estrogen-progestin daily therapy for 4 years or more was calculated to be 3.68 (CI = 2.14-6.34). Sequential estrogen-progestin therapy had a risk of 2.81 (CI = 1.57-5.08). The use of estradiol without progestins was reported to have no increased risk.

COMMENT BY LEON SPEROFF, MD

These results, highlighted in the media, are no different than those recently reported by the Women's Health Initiative. One could argue that this Swedish study is more impressive because the size of the risks associated with estrogen-progestin therapy is much larger, but there are problems with the study that make such a conclusion a little shaky.

The strength of the study is in the size of the cohort and the prospective design. Added to that is the ability to accurately track individuals in Sweden through a comprehensive registry system. Nevertheless, there are several problems. The risk ratios are calculated by comparing the observed number of cases with an expected number based upon the reference data in the government registries. Therefore, hormone users were not compared to nonusers; both users and nonusers were compared to expected outcomes. This is not a bad technique, but it provides approximations not absolutely accurate determinations.

The study carefully adjusted for many factors that affect the risk of breast cancer, including age of menarche, age at menopause, age at first full-term pregnancy, parity, and age at diagnosis. However, there are at least 4 more critical influences that were unaccounted for: use of mammography, presence of benign breast disease (specifically with atypical hyperplasia), body size, and alcohol intake.

The specific estrogen and progestin drugs were not identified, but in Sweden we know that the most popular regimen is composed of estradiol and norethindrone. This at least is evidence that American reports based mainly on the use of conjugated equine estrogens and medroxyprogesterone acetate do not indicate results limited to one formulation.

As in the Women's Health Initiative, the appearance of an increased risk by 4 years of use is relatively rapid. This is consistent with an effect on pre-existing tumors. Therefore, the recent data have not answered our most fundamental question: is there a slightly increased risk of breast cancer with combined estrogen-progestin postmenopausal therapy or are we seeing the results of earlier detection of tumors because of effects on pre-existing tumors? The now well-recognized better survival rates in postmenopausal women who develop breast cancer while on hormone therapy argues in favor of an effect on pre-existing tumors.

The good news is that the Swedish study reported no increase in risk associated with the use of estrogen alone. This is the reason that the estrogen-only arm of the Women's Health Initiative has not been discontinued. Only time will tell if estrogen-only is a different story. ■

Dr. Speroff is Professor of Obstetrics and Gynecology, Oregon Health Sciences University, Portland, Ore.

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International Collaborative Ovarian Neoplasm Trial 1 and Adjuvant Chemotherapy In Ovarian Neoplasm Trial

ABSTRACT & COMMENTARY

Synopsis: *Platinum-based adjuvant chemotherapy improved overall survival and recurrence-free survival at 5 years in this combined group of patients with early-stage ovarian cancer defined by the inclusion criteria of the ICON1 and ACTION trials.*

Source: International Collaborative Ovarian Neoplasm 1 [ICON1] and European Organisation for Research and Treatment of Cancer Collaborators-Adjuvant ChemoTherapy In Ovarian Neoplasm [EORTC-ACTION]. *J Natl Cancer Inst*. 2003;95: 105-112.

The investigators of 2 major and parallel European randomized clinical trials focused on early-stage epithelial ovarian cancer (International Collaborative Ovarian Neoplasm 1 [ICON1] and Adjuvant ChemoTherapy In Ovarian Neoplasm [ACTION] performed a combined analysis. Both trials compared platinum-based adjuvant chemotherapy with observation following primary surgery. Between 1990 and 2000, 925 patients (477 in ICON1 and 448 in ACTION) who had surgery for early stage ovarian cancer were randomly assigned to receive platinum-based adjuvant chemotherapy (n = 465) or observation (n = 460) until chemotherapy was indicated. After a median follow-up of more than 4 years, 245 patients had died or had a recurrence (ICON1: 33, ACTION: 112). Overall survival at 5 years was 82% in the chemotherapy arm and 74% in the observation arm (difference = 8%; [95% confidence interval (CI) = 2-12%]; hazard ratio [HR] = 0.67; 95% CI = 0.50-0.90; P = .008). Recurrence-free survival at 5 years was also better in the adjuvant chemotherapy arm than it was in the observation arm (76% vs 65%; difference = 11% [95% CI = 5-16]; HR = 0.64; 95% CI = 0.50-0.82; P = .001). Subgroup analysis provided no evidence of a difference in the size of effect of chemotherapy on survival in any pretreatment subcategory (age, tumor stage, histologic cell type, and differentiation grade). The trial concluded that platinum-based adjuvant chemotherapy improved overall survival and recurrence-free survival at 5 years in this combined group of patients with early stage ovarian cancer defined by the inclusion criteria of the ICON1 and ACTION trials .

COMMENT BY DAVID M. GERSHENSON, MD

Approximately 30% of women with epithelial ovarian cancer have stage I or II disease. Although the overall survival of patients with stage I disease is 80-90% and the overall survival of patients with stage II disease is 50-70%, there is still a wide range of survival times for various subsets of patients within this category. Over the past 2 decades or so, experts have been able to reach a consensus on the definition of "high-risk" early stage disease that is associated with a worse outcome. Most agree that high-risk early stage ovarian cancer includes stage Ia and Ib, grades 2 and 3; all clear cell carcinomas; and all stages Ic and II. There has been a difference in philosophy between the American and the European perspective regarding the conduct of early stage ovarian cancer trials. The Europeans have maintained historically that, prior to the findings of these trials, there was no evidence of benefit from adjuvant therapy; thus, their clinical trials, as demonstrated by these studies, have generally included a comparison of treatment vs observation. On the other hand, the Americans have made the assumption that the prognosis of high-risk early stage patients is not so wonderful, thereby choosing to design trials comparing 2 different treatments. Now that these trials have seemingly established the benefits of adjuvant therapy once and for all, most future trials will assume the American design. However, as always, the details are important. In the ICON1 trial, patients with well-differentiated tumors and stage III disease were included. In the ACTION trial, where eligibility criteria were more restrictive, the benefit of adjuvant chemotherapy was limited to patients with nonoptimal staging. Of course, this just underscores the fact that all clinical trials have flaws—some more major than others. In this case, the true value of adjuvant chemotherapy for patients with high-risk early stage ovarian cancer still remains somewhat uncertain. The goal of future trials will be to tease out those patients who do not require adjuvant treatment, and most of us believe that the identification of these good-prognosis patients will be based on some, as yet unknown, molecular biomarker. ■

Dr. Gershenson is Professor and Chairman, Department of Gynecology, M.D. Anderson Cancer Center, Houston, Tex.

CME Questions

12. In the treatment of elderly patients with non-small-cell lung cancer, the selection of which of the following regimens would *not* be recommended based upon findings from the ELVIS and MILES trials?

a. Single-agent vinorelbine
b. Single-agent gemcitabine
c. Combined vinorelbine and gemcitabine
d. All of the above

13. Regarding the treatment of advanced pancreatic cancer with chemotherapy, which of the following approaches reflects the standard of care?

a. Gemcitabine administered as a single agent
b. Gemcitabine and infusional 5 fluorouracil
c. Gemcitabine and oral capecitabine
d. Oral capecitabine administered as a single agent

14. In the Lee et al brachytherapy paper:

a. both sides of the resection bed were typically implanted.
b. postoperative implants typically led to problems with fistulas.
c. postoperative implants were easily accomplished through thoracoscopy ports.
d. mediastinoscopy was routinely performed to facilitate patient selection.

15. Regarding the Lee et al brachytherapy paper, which statement is correct?

a. Complications were most apt to occur in reirradiated patients.
b. Suture line hemorrhage or necrosis occurred in 20% of patients.
c. I-125 seeds were used to generate 50-100 Gy to the target volume.
d. The local control rate in T1 patients was about 90%.

16. The following statements are true regarding postmenopausal hormone therapy and the risk of breast cancer *except*:

a. An increased risk of postmenopausal breast cancer has been reported with the use of more than 1 type of progestin.
b. The appearance of breast cancer in postmenopausal hormone users is relatively slow.
c. Thus far, most studies have not found an increased risk of breast cancer associated with the use of unopposed estrogen.
d. Postmenopausal estrogen-progestin therapy may cause earlier detection of breast cancer by affecting pre-existing tumors.

Answers: 12 (c); 13 (a); 14 (a); 15 (d); 16 (b)

In Future Issues:

Variations in Lung Cancer Risk Among Smokers