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CLINICAL ONCOLOGY ALERT™

A monthly update of developments in cancer treatment and research

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Role of Laparoscopy in the Management of Pancreatic Cancer

ABSTRACT & COMMENTARY

Source: Luque-de Leon E, et al. *J Gastrointest Surg* 1999;3:111-118.

Laparoscopy is commonly used to stage patients with pancreatic cancer and to determine resectability. In a retrospective analysis from the Mayo Clinic presented by Luque-de Leon and colleagues, an argument is presented that the role of laparoscopy be expanded to determine palliative approaches for patients with unresectable lesions.

The clinical series reviewed included those patients treated at the Mayo Clinic between 1985 and 1992 who were felt to have resectable pancreatic cancer on the basis of state-of-the-art imaging techniques, but who were found to have unresectable lesions at surgery. Data were available for 148 such patients. All were considered resectable preoperatively but, at the time of surgery, 29 (20%) were found to have liver metastases (Group I), 22 (15%) had peritoneal dissemination (Group II), 44 (33%) had metastatic lymph nodes (Group III), and 53 (35%) had locally advanced disease with vascular involvement (Group IV). Overall median survival was nine months, but survival varied significantly among the groups. Groups I and II each had a median survival of six months, whereas Groups III and IV each had a median survival of 11 months.

These patients were evaluated by the currently used practice of staging laparoscopy. Luque de-Leon et al discuss the role that laparoscopy could play in addition to determining which patients have resectable cancers. They propose that patients with laparoscopically detected unresectability on the basis of hepatic metastases or peritoneal dissemination have a poor prognosis and might best be treated with nonoperative approaches, such as endoscopically placed endobiliary stents. In contrast, for those patients with metastatic nodes, or locally advanced tumors with vascular invasion (Groups III or IV above) in whom median survival approaches one year, operative palliation with biliary and duodenal bypass combined with operative chemical splanchnicectomy (ablation of splanchnic vessels) might offer better palliation. Thus, they argue that the role of staging laparoscopy should not be just to improve the resectability rate, but to define a group of patients with unre-

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sectable lesions who might still benefit from a palliative operative procedure.

COMMENTARY

In the great majority of patients with pancreatic cancer, the tumor is unresectable at the time of presentation. Although laparoscopy is not a new approach, technical advances have allowed for more widespread usage and it is now frequently used in staging evaluation to assist in the determination of resectability. For example, by using an "extended" laparoscopic evaluation, Conlon and colleagues viewed the lesser sac, porta hepatis, duodenum, transverse mesocolon, and celiac and portal vessels by laparoscopy before surgery. They reported positive and negative predictive indices of 100% and 91%, respectively, and their resectability rate rose to an impressive 76%.[1]

Luque-de Leon et al argue that high resectability rates should not be the only goal of staging laparoscopy. Instead, they propose that the procedure be used to define optimal palliative approaches based upon the survival data presented for the different laparoscopically determined reasons for unresectability. The argument is difficult to refute. Nonetheless, endoscopists might point to the rapidly advancing technology in endoprostheses (e.g., self expanding metallic stents) that could allow for more long-lasting palliation, comparable to surgical bypass but without surgical morbidity.[2] Also, the developing technique of laparoscopically performed biliary-enteric bypass may provide yet another role for laparoscopy in these patients.[3]

It should be kept in mind that the data presented in this series were for head of the pancreas lesions alone. For patients with cancers in the body or tail, operative palliation is not usually necessary and laparoscopy remains a procedure used only to establish resectability.

This published report from the Mayo Clinic offers useful guidelines for the evaluation and treatment of patients considered operative candidates based upon a good performance status and a periampullary mass demonstrated by CT and/or endoscopic retrograde cholangiopancreatography (ERCP). If laparoscopy in such patients demonstrates peritoneal dissemination or hepatic metastases, endobiliary stent with or without celiac plexus block would be a reasonable approach. If neither peritoneal dissemination nor hepatic involvement is found, exploration is recommended. For those found to have unresectable lesions, bilioenteric bypass, gastrojejumnostomy, and chemical splanchnicectomy could provide durable palliation for what might be expected to be a median survival of approximately one year. ❖

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Raloxifene and the Prevention of Breast Cancer

ABSTRACT & COMMENTARY

Synopsis: *The Multiple Outcomes of Raloxifene Evaluation is a large, multicenter trial of the antiestrogen, raloxifene, in postmenopausal women with osteoporosis. Breast cancer incidence was reduced by 76% in the groups receiving raloxifene. Raloxifene increased the risk of venous thromboembolic disease but did not increase the risk of endometrial cancer.*

Source: Cummings SR, et al. *JAMA* 1999;281: 2189-2197.

Raloxifene hydrochloride is a selective estrogen receptor modulator (SERM) that has anti-estro-

genic effects on breast and endometrial tissue and estrogenic effects on bone, lipids, and coagulation proteins. Cummings and colleagues report the results of a large clinical trial of this agent in postmenopausal, osteoporotic women with the outcome of interest being the development of breast cancer.

The Multiple Outcomes of Raloxifene Evaluation (MORE) study included a total of 7705 postmenopausal women, younger than 81 years (mean age, 66.5 years) with osteoporosis, defined by the presence of vertebral fractures or femoral neck or spine T-score of at least 2.5 S.D.s below the mean for young healthy women. Women with a history of breast cancer or who were taking estrogen were excluded. Enrolled volunteers received two pills per day. They would receive either raloxifene 60 mg twice a day, raloxifene 60 mg once a day and placebo once per day, or placebo twice a day. Of the 5129 women who received raloxifene, 13 cases of breast cancer occurred over the three years of the study. In contrast, there were 27 cases among the 2576 women assigned to placebo (relative risk, 0.24; 95% confidence interval, 0.13-0.44). Raloxifene decreased the risk of estrogen receptor-positive breast cancer by 90%, but had no apparent effect upon the development of estrogen receptor-negative, invasive breast cancers.

In this study, raloxifene was generally well tolerated. The primary untoward effect was hot flashes, but compliance remained high, and the rate of patients withdrawing from study was comparable among the three groups.

There was no increased endometrial cancer in the raloxifene-treated women, although there was a slightly increased endometrial tissue thickness by transvaginal ultrasonography (performed on a subset of volunteers, n = 1781). However, there was an increase in the risk for thromboembolic disease. By 40 months of follow-up, there was a higher rate of deep venous thrombosis (38 cases, 0.7%) and pulmonary embolus (17 cases, 0.3%) in the raloxifene-treated individuals when compared to the placebo control group (5 cases of venous thrombosis, 0.2% and 3 cases, 0.1% of pulmonary embolus).

Thus, among postmenopausal women with osteoporosis, the risk of invasive breast cancer was decreased by 76% during the three years of treatment and the toxicity was considered manageable.

COMMENTARY

The prototype anti-estrogen, tamoxifen, was shown in the Breast Cancer Prevention Trial (BCPT) to be effective in the primary prevention of breast cancer in high-risk individuals (older, with family history, etc.).[1] In a group of patients with a risk of about 1.66% or greater in five years, based on their individual profile of prognostic factors, the risk of developing breast cancer was reduced by about 50% by tamoxifen. Although earlier, smaller studies had failed to show any benefit for tamoxifen in primary prevention, there is confidence in the BCPT findings because of the scope and size of the study and the robust findings.[2,3] Enthusiasm for the development of alternative anti-estrogens was based upon some of the toxicity of long-term tamoxifen treatment, including deep vein thrombosis and endometrial cancer. Raloxifene offers the theoretical advantage of having anti-estrogenic functions at the endometrium (and breast) while functioning as an estrogen agonist at bone.[4]

This clinical trial, conducted at 180 centers in 25 countries (but mainly in the United States and Europe) effectively evaluated a large number of patients by using a fairly simple clinical trial design. Individuals were not at unusually high risk for breast cancer, except for their age. They were not selected for family history or by other risk factors. In fact, breast cancer has been reported to be less common in women with osteoporosis, perhaps related to their more complete or long-standing estrogen-deficient status. Yet, once again, a robust reduction in the development of new cancers was observed. As expected, no enhanced endometrial cancer was observed. There was an increase in deep venous thrombosis and pulmonary embolus. Although data were not shown in this regard, the individuals enrolled on this trial (all with significant osteoporosis) did have decreased vertebral fracture (but not fracture at other sites). Thus, raloxifene may prove to be more useful than tamoxifen in the primary prevention of breast cancer. It appears that its efficacy is at least comparable, and it may be better tolerated (with less endothelial proliferation) than tamoxifen. Comparisons in other aspects of health are also needed. Will raloxifene have the same (or better) salutory effects on serum lipids and cardiovascular end points? None of the anti-estrogens have been evaluated for their effect on cognitive function, yet hormone replacement therapy has been shown to promote cognitive function and reduce the incidence of Alzheimer's disease. Will the anti-estrogens and SERMs promote cognitive decline? Longer term and more comprehensive studies are needed to determine if this reduction in breast cancer incidence will be diminished with time as the estrogen-receptor-bearing tumors become resistant to the hormonal intervention and to evaluate the influence of the intervention on all-cause morbidity and mortality. ❖

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The Value of Postmastectomy Radiation for Cancer Patients at Risk for Local Recurrence

ABSTRACTS & COMMENTARY

Synopsis: *There remains some controversy regarding the use of postmastectomy radiation therapy. In this report from the University of Pennsylvania, the outcomes of high-risk patients (those with large primary tumors, close or involved surgical margins, or axillary nodes positive) treated between the years 1977-1992 were detailed. The data support the use of this modality for high-risk patients.*

Sources: Metz JM, et al. *Cancer J Sci Am* 1999;5: 77-83. Pierce LJ. *Cancer J Sci Am* 1999;5:70-72.

There remains some controversy on the value of postmastectomy radiation therapy in the treatment of breast cancer. With regard to patients at high risk for recurrence after mastectomy, the controversy relates to the balance of increased toxicity vs. improved disease control and overall survival. In this report from the University of Pennsylvania, Metz and colleagues report their long-term experience in treating such patients.

Over a 15-year period (1977-1992), 221 patients at high risk for local-regional recurrence after mastectomy were treated with radiation therapy, with or without adjuvant hormonal or chemotherapy. The median age was 51 years. Patients were classified as high-risk because of T3 or T4 tumors, positive lymph nodes, or close or positive surgical margins. Radiation therapy consisted of 45-50.4 Gy to the chest wall in 1.8-2.0 Gy fractions. Regional lymph nodes were also treated with radiation therapy in 85% of the cases. Of the 221 cases, 151 (68%) received adjuvant chemotherapy. Patients receiving adjuvant chemotherapy were younger (median age 48, compared to a median age of 64 for those who did not receive chemotherapy) and had a greater degree of axillary node involvement (median 5 nodes vs 1). Adjuvant hormonal therapy was administered to 116 patients (53%). The median follow-up was 4.3 years.

In the overall group, the actuarial local-regional failure rate at 10 years was 11% (95% CI 6.5%-16.7%). The site of first failure was distant metastases in 75 patients (34%), local-regional recurrence in 11 patients (5%), and coincidental local-regional and distant in three patients (1%). Of the 11 patients who developed local-regional recurrence as the site of first-treatment failure, that recurrence developed at a median of 1.3 years, and nine (82%) subsequently developed systemic metastases.

Metz et al conclude that their experience supports the continued use of postmastectomy radiation therapy for patients at high-risk for local-regional recurrence.

COMMENTARY

Recommendations about the use of radiation therapy after mastectomy have varied over the years, but these days its use is common, particularly in those at high risk for local-regional recurrence. The downside, of course, is the fear of toxicity, primarily to the heart as evidenced in a number of clinical trials.[1,2] Other risks include rib fractures and late second solid tumors. Patients at high risk are typically candidates for chemotherapy as well and agents commonly in use (anthracyclines, taxanes, and possibly Herceptin) may potentially enhance cardiotoxicity.

Nonetheless, enthusiasm for radiation treatment in this setting has re-emerged with the publication of two randomized trials (from Denmark and British Columbia) in recent years.[3,4] In these studies, both disease-free and overall survival were enhanced by the addition of postmastectomy radiation therapy. The survival advantage was initially more evident in the Danish study and was only marginally significant in the British Columbia analysis. However, a recent update of the British Columbia study (at 15 years) now clearly demonstrates a survival advantage for those who received radiation therapy.[5] A recent update of the Danish study, with a median of 10 years of follow-up, confirms the earlier results.[6] Postoperative radiation therapy reduces the risk of recurrence, which leads to improved survival.

As pointed out by Dr. Pierce in her editorial review, the value of the University of Pennsylvania series (as reported by Metz et al) may lie in its comprehensive detailing of treatment technique and outcomes in a series from a single institution. Although some persisting questions, such as the necessity for treatment of the internal mammary nodes, could not be addressed satisfactorily in this series, the report did lend sufficient confidence that radiation therapy can be delivered safely with acceptable toxicity, and result in enhanced long-term survival for high-risk patients. ❖

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Gemcitabine and Carboplatin: A Well-Tolerated Active Combination for Advanced Non-Small-Cell Lung Cancer

ABSTRACT & COMMENTARY

Synopsis: *Chemotherapy has been shown in a number of studies to enhance survival and quality of life in non-small-cell lung cancer, but the effects are small. The current trial investigates the use of escalating doses of gemcitabine in combination with a standard dose of carboplatin in previously untreated patients with advanced lung cancer. Median duration of response was 13 months and overall survival was 16 months.*

Source: Iaffaioli RV, et al. *J Clin Oncol* 1999;17: 921-926.

Developing new chemotherapy regimens for the treatment of advanced lung cancer has been the subject of research for many investigative teams in clinical oncology. This work is predicated upon the demonstration of enhanced quality-of-life and survival with certain regimens, particularly those that include cisplatin.[1,2] The thrust to develop new regimens derives from the only modest enhancement of survival by the currently used standard regimens. The purpose of the current study was to examine gemcitabine and carboplatin in a combination phase I-II study in patients with stage IIIB and IV non-small-cell lung cancer. The selection of these drugs was based on earlier work that indicated gemcitabine to have significant single-agent effects in lung cancer and the absence of nausea from carboplatin when compared to cisplatin.[3] Gemcitabine is relatively less myelotoxic than some other active agents and might even synergize with carboplatin.

Chemotherapy-naive patients with advanced lung cancer received carboplatin at a single dose (AUC 5 mg/mL/min) and gemcitabine at an initial dose of 800 mg/m^2, subsequently escalated by 100 mg/m^2 per step. Gemcitabine was administered on days 1 and 8 and carboplatin on day 8 of a 28-day cycle.

Neutropenia was the dose-limiting toxicity, and it occurred in three of five patients receiving gemcitabine at 1200 mg/m^2. Nonhematologic toxicities were mild. Thus, the recommendation for future phase II trials includes a dose of gemcitabine at 1100 mg/m^2 with carboplatin AUC 5.

Although it was not the goal of the current study to establish efficacy, it was noted that 13 of 26 patients had either a partial (35%) or complete (15%) response. The median duration of response was 13 months (range, 3-223 months) and the median overall survival was 16 months (range, 3-226 months). These figures compare favorably with other, perhaps more toxic regimens and thus, there is anticipation that this new combination may be a step forward in the treatment of advanced lung cancer.

COMMENTARY

This clinical investigation by Iaffaioli and colleagues sets the stage for future trials of an interesting regimen. The primary end point of the current trial was simply to define for future investigations the recommended dose of gemcitabine when used in combination with carboplatin. Nonetheless, the impressive response rate, particularly with regard to duration of response and median overall survival, is hard to ignore. Of course, one has to use caution when making phase II conclusions from phase I data, but at least it can be said that the combination looks encouraging.

With regard to toxicity, it appears that the combination of gemcitabine and carboplatin is acceptable. Gemcitabine, with only modest hematologic toxicity, is apparently combined safely with carboplatin, particularly on the schedule used. In this regard, it is encouraging to note that no dose reductions were required and no patients were withdrawn from study due to failure to achieve hematologic recovery. Approximately 25% of the treatment courses were delayed by one week due to neutropenia or thrombocytopenia, but the protocol was not abandoned by any patient who reached the gemcitabine dose of 1100 mg/m^2 because of marrow toxicity.

Furthermore, the nonhematologic side effects were encouragingly mild. Only two of the 26 patients reached a grade 3 level of nausea and vomiting. Alopecia was common but all nonhematologic toxic effects were of short duration after treatment interruption. Thus, it is difficult to find fault with the conclusions of Iaffaioli et al that this combination of gemcitabine and carboplatin is worthy of further study. If the phase II trials that are currently underway substantiate these early

indicators of efficacy, it will be a regimen that will soon be investigated for front-line treatment of advanced lung cancer. ❖

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Special Feature

Update in Palliative Care XI: Beyond Pain

By Thomas J Smith, MD, FACP

George soros, the richest man in the world, watched his wife die of breast cancer. She was in pain, mostly ignored, or not ministered to by doctors who could have chosen to be there. There were no discussions about advanced directives, or prognosis and expectations. Having billions to give away, he started the Project on Death in America, in an attempt to change for the better how Americans die. He hired Kathy Foley to direct it, and he chose about 20 people a year for aid.

Now the AMA has started the Education for Physicians on End of Life Care (EPEC), from which I just returned. ASCO also plans a half-day symposium in 2000 at the annual meeting. Sign up for either, or both, if you get a chance.

I was initially unconvinced that palliative care was a specialty. After all, didn't we all know how to give morphine? Well, actually not, given that more than half of the patients in academic hospitals died with unrelieved pain—palliative care works, and some people do it better than others.

Think back over the last 10 patients you have had die at home or in the hospital, and what distressed them or their families. Here is some of what I have learned in my three years.

Delirium is Common and Treatable

Ask a hospice nurse, and you will find that "terminal delirium" is one of the most common and troubling problems that distresses families with relatives near death. Moaning and delirium is upsetting to watch and is often interpreted as pain. But it's not pain, and high accumulations of narcotics due to diminished renal clearance may be one of the most common causes. (*See Table 1.*)

Table 1

Troubleshooting in Terminal Delirium Cases

Cause	Solution
Too much narcotic	Don't stop it! Just cut it in half. If that does not work, then stop it.
Too little renal clearance	In the patient with weeks to live consider a trial of hydration, with a switch to another narcotic at equivalent doses.
No definable reason	Reassure the family that it is a common pre-terminal event.Reassure them that it is not pain. Don't treat unless it bothers someone. Who knows what they are seeing.*

**Haloperidol (0.25-1.0 mg syrup in the cheek, or rectal) works much better than benzodiazepines.*

Agitation is Common and Treatable, too

Again, haloperidol wins hands down over benzodiazepines, when studied. It has a good anti-emetic effect and probably accounts for fewer falls and fractures. Start low at 0.25 mg or so and work up.

Terminal Nausea is Common and Treatable

No one really knows why, but it is common. And the best solutions are not XYZ-tron at $60 a day. Use a dopamine-receptor drug, such as metaclopramide 10-30 mg q 6 h, and some dexamethasone. It has the added advantage of enhancing bowel motility, too. (These tablets can be added to a suppository.) If that fails, try haloperidol 0.5-1.0 mg q 6 h or droperidol. If that doesn't work, try another class of agents such as the serotonin receptor drugs (granisetron, ondansetron, etc.) or a benzodiazepine.

Terminal Dyspnea is Treatable

No need to be fancy here. Any narcotic will do if given as for pain, around-the-clock, and at the dose that works. Morphine works to reduce the work of breathing by relaxing the lung smooth muscle. Start with 5-10 mg q 4 h and titrate up to comfort, just like with pain. There is typically little or no effect on respiratory rate. Don't start with pulse oximetry and ABGs since the goal is to relieve the suffering of labored breathing; it's easier to not start them than to take them away once established.

If that does not work, try a fan blowing air across the patient (I know it sounds too simple, but try it once—it

works). Then, oxygen (but remember it's expensive and hard to stop) then try steroids (and next) benzodiazepines. For some patients, it takes a combo of morphine and benzodiazepines. Inhalers such as albuterol rarely work and are not worth trying.

Nebulized morphine/fentany/etc. had a brief run of popularity. And it works, but no better than nebulized saline in randomized clinical trials. It's the narcotic, and we might as well give it P.O. or P.R.

The "Death Rattles"

This is the number one reason panicked families call me or hospice nurses. The dying person is usually in no distress, but it's hard to watch. (*See Table 2*.)

Table 2

Alleviating the "Death Rattle"

Cause	Treatment
Ineffective clearance	Prop the patient up and to his/her side.
Too many secretions	Scopolamine patches, just like for seasickness. Rarely cause disorientation in the terminally ill (or hard to tell) but can cause problems in the frail elderly who are still mobile. Put them on before it gets too bad because it's easier to prevent.

Depression is the Norm, not the Exception

Depression can be hard to differentiate from the sadness and grief of dying. I have switched to the "Chochinov Test" of Dr. Harvey Chochinov:

"Are you Depressed?"

If the patient says no, or "Yes, this is terrible! I'm dying, and feel so hopeless, and I don't have the energy to get up and I can't sleep...." you have more than an 80% chance of being right in your diagnosis. Plus, you asked.

Typical anti-depressants can work but may take weeks. Start them or get a psychiatric consultation (tough for the homebound). Consider starting a short course of methylphenidate (Ritalin) or some other stimulant at low doses (e.g., 2.5-5 mg in the morning and at noon) increasing to tolerance. This also works for the morphine patient who cannot wake up.

Dr. Kevorkian, the Pinata of Palliative Care

Dr. Chochinov noted in his sample of 200 dying patients that nearly one in 10 had clinical depression. Of those requesting euthanasia, six of 10 were depressed. Almost all the requests for physician-assisted suicide (PAS) came from the depressed group. Most of these requests changed after about two weeks. I won't go over the six-step program to manage PAS, but someone's clever phrase was too hard to pass up.

Hiccups

Antacid with simethicone (then try) metaclopramide 10-30 mg q 4-6 h (or cisapride 20 mg q 12 h, but try the low priced spread first) (and next) baclofen 5-10 mg q 6-12 h.

Chlorpromazine, the drug most often used, is too sedating and rarely effective. Don't use prochlorperazine (Compazine) with metaclopramide (Reglan), as the first will block the prokinetic movement of the second and will increase the chance of extra pyramidal side effects.

Myoclonic Jerks

"Well, doctor, you've finally gotten him comfortable but he's jerking all over as soon as he drifts off to sleep, do something about those seizures!"

Myoclonic jerks ("sleepstarts") are normal and can happen with any narcotic. I have listed some of the most common causes and solutions here. Reassure the patient/family that these are not seizures, and only require treatment if bothersome. These movements are so characteristic that no diagnostic testing is needed other than a good clinician! (*See Table 3*.)

Table 3

Treating Myoclonic Jerks

Cause	Solution
Normal reaction to narcotic	Reassurance. Benzodiazepine (e.g., lorazepam 0.5-1 mg q 12 h, clonazepam, or diazepam.) Consider a switch to a new narcotic, which can give a "honeymoon" period of several weeks.
Hyponatremia or renal failure	Only treat if indicated.

This isn't Rocket Science, but there isn't a lot of Science being done about it

The ASCO abstracts on palliative care this year were heavily skewed to fatigue, vomiting, and pharmaceutical interventions. Most of the above-mentioned material has been known for about 10 years but had not trickled down to mainstream oncologists like me.

There are some great places to learn more about these programs. Check out the EPEC website (http://www.ama-assn.org/ethic/epec/) or address (The EPEC Project, Institute for Ethics, American Medical Association, 515 N. State Street, Chicago, IL 60610, 312-464-4979) and sign up for a course. Much of it is

old hat to oncologists, but a great refresher, and a way to then teach our colleagues in medicine, family practice, and surgery to practice these procedures. After all, we want them here for us when we die.

Take Home Message

First, when someone is dying, call hospice six weeks before they are dead, not six hours.

Second, when someone is dying, there is a lot you can do about it. Yes, I know it's not reimbursed well, and it's harder than choosing between Taxol and Taxotere, but this is why most of us chose to become doctors.

You can make the difference between a peaceful planned death at home, or a traumatic death that includes uncontrolled pain, ER visits, late night phone calls, and disgruntled family members. Either will be long remembered—it's our choice. ❖

Suggested Reading

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CME Questions

5. With regard to staging laparoscopy for patients with cancers at the head of the pancreas, which of the following statements is true?

a. When used solely to determine resectability, the procedure is very effective at reducing the rate of operative determination of unresectability.
b. The procedure is dangerous in patients with hepatic metastases, and should not be performed in patients with elevated liver function tests.
c. When hepatic peritoneal dissemination is demonstrated, median survival is about one year and surgical palliation is warranted.
d. When vascular invasion is demonstrated, median survival is about six months and endoscopic, but not surgical, palliation is indicated.
e. Laparoscopy is inferior to laparotomy in the performance of palliative biliary bypass procedures.

6. In developing a primary breast cancer prevention strategy, raloxifene offers a theoretical advantage over tamoxifen based upon:

a. its proven superiority in preventing estrogen-receptor breast cancer.
b. its reduced stimulatory effect on the uterine endometrium and, therefore, a reduced potential to induce endometrial cancer
c. its proven superiority in preventing bone loss in patients with breast cancer.
d. its better tolerability and greater patient compliance profile
e. its lower likelihood of inducing deep venous thromboses and pulmonary emboli.

7. Which of the following statements about post mastectomy radiation therapy for patients at high risk for recurrence is false?

a. Local-regional recurrence rates have been shown in a number of series to be reduced.
b. Disease-free survival has been shown to be enhanced in treated patients.
c. Potential cardiac toxicity precludes the adjuvant use of anthracyclines or taxanes.
d. Patients who later develop local recurrence have a high incidence of systemic disease within a short time interval.
e. Overall survival is improved by post mastectomy radiation therapy.

8. Which one of the following statements about the use of gem citabine with carboplatin for advanced lung cancer is true?

a. It is now established as front-line therapy for previously untreated patients.
b. The combination has an acceptable toxicity profile, and has been established by phase II trials to be highly effective.
c. The combination has an acceptable toxicity profile, but phase II trials need to be completed before it should be widely used in this setting.
d. The combination has an unacceptable toxicity profile, and future studies of its efficacy are not warranted.
e. The combination has an acceptable toxicity profile, but does not appear to be sufficiently active to warrant additional study.

In Future Issues:

Continuous Infusions of Doxrubicin and Paclitaxel in Refractory Ovarian Cancer