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Chemotherapy for Non-Small-Cell Lung Cancer: Are We Making Progress?

ABSTRACT & COMMENTARY

Synopsis: *A prospective, randomized study was conducted to compare 3 experimental chemotherapy regimens with a reference regimen of cisplatin and paclitaxel for patients with advanced non-small cell lung cancer. A total of 1207 patients (1155 eligible) were randomly assigned to receive cisplatin and paclitaxel, cisplatin and gemcitabine, cisplatin and docetaxel, or carboplatin and paclitaxel. The overall response rate for all eligible patients was 19%, with a median survival of 7.9 months (95% confidence interval, 7.3-8.5 months). While differences in toxicity profiles were demonstrated, none of the 4 regimens offered a significant advantage over the others for overall survival.*

Source: Schiller JH, et al. *N Engl J Med*. 2002;346(2):92-98.

Non-small-cell lung cancer is a common disease and a leading cause of death from cancer.[1] The prognosis for patients with untreated metastatic non-small-cell lung cancer is extremely poor, with median survival of approximately 5 months and 1-year survival rates around 10%.[1] The results of chemotherapy for the treatment of patients with metastatic non-small-cell lung cancer have been disappointing. While several studies have demonstrated a small survival improvement with chemotherapy for patients with advanced non-small-cell lung cancer, the magnitude of benefit has been small.[2,3] Chemotherapy has been shown to improve symptoms and improve quality of life when compared with "best supportive care."[4] Thus, numerous chemotherapy regimens have been developed for patients with advanced non-small-cell lung cancer. Uncontrolled Phase II studies have suggested high response rates as well as prolonged survival with several of these regimens. Thus, a randomized, clinical study was needed to compare overall survival of non-small-cell lung cancer patients following treatment with a reference chemotherapy regimen (cisplatin and paclitaxel) or with newer regimens including cisplatin and gemcitabine, cisplatin and docetaxel, and carboplatin and paclitaxel.

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The study by Schiller and associates was a prospective, randomized study of 1207 patients with advanced non-small-cell lung cancer. Eligible patients had non-small-cell lung cancer that was Stage IIIB (with malignant pleural or pericardial effusion), stage IV, or recurrent disease, and received 1 of 4 treatments. The cisplatin and paclitaxel regimen consisted of 135 mg of paclitaxel/m^2 of body surface area administered over a 24-hour period on day 1, followed by 75 mg of cisplatin/m^2 on day 2. The cycle was repeated every 3 weeks. The cisplatin and gemcitabine regimen consisted of gemcitabine at a dose of 1000 mg/m^2 administered on days 1, 8, and 15; and cisplatin at a dose of 100 mg/m^2 administered on day 1 of a 4-week cycle. The cisplatin and docetaxel regimen consisted of docetaxel at a dose of 75 mg/m^2 and cisplatin at a dose of 75 mg/m^2 on day 1 of a 3-week cycle. The carboplatin and paclitaxel regimen consisted of paclitaxel at a dose of 225 mg/m^2 over a 3-hour period followed by carboplatin at a dose calculated to produce an area under the concentration-time curve of 6.0 mg/mL/min on day 1 of a 3-week cycle. Stratification variables include performance status, weight loss in the previous 6 months, stage IIIB vs. IV or recurrent disease, and presence or absence of brain metastases. Patient characteristics including age, sex, performance status, brain metastases, weight loss, race, and disease stage were well balanced among treatment groups. There were a similar number of ineligible patients in each of the treatment groups. The overall outcome for all eligible 1155 patients was a response rate of 19%, median survival of 7.9 months, 33% 1-year survival, 11% 2-year survival, and a median time to progression of 3.6 months. These results were not significantly different from the results for all 1207 randomized patients. There was no significant difference in overall survival between any of the 3 experimental treatment groups and the reference group receiving cisplatin and paclitaxel. Median survival for patients receiving cisplatin and paclitaxel was 7.8 months (range, 7.0-8.9 months). Median survival following treatment with cisplatin and gemcitabine was 8.1 months (range, 7.2-9.4 months); cisplatin and docetaxel was 7.4 months (range, 6.6-8.8 months); and carboplatin and paclitaxel was 8.1 months (range, 7.0-9.5 months). Similar results were seen in all groups with the percent of patients alive at 1 and 2 years, and results with cisplatin and paclitaxel achieved a 1-year survival of 31% (CI, 26-36) and a 2-year survival of 10% (CI, %). There was a statistically significant increase in median time to progression with the cisplatin and gemcitabine group. However, this time to progression was 4.2 months (range, 3.7-4.8 months), and this was marginally improved from the 3.4-month median time to progression in the cisplatin and paclitaxel group (range, 2.8-3.9 months). However, no difference in overall survival was seen between these groups. Differences in toxicities were seen following treatment with the different regimens. Cisplatin and gemcitabine appeared to be more toxic than cisplatin and paclitaxel. There were more Grade 3 and Grade 4 renal toxic effects, more anemia and thrombocytopenia, but less febrile neutropenia with cisplatin and gemcitabine than with cisplatin and paclitaxel. The regimen of carboplatin and paclitaxel had significantly fewer overall grade 4 and 5 toxic events when compared with cisplatin and paclitaxel. Schiller et al concluded that no advantage in survival is achieved with any of the 4 commonly used regimens. The regimen of carboplatin and paclitaxel was selected as a reference regimen for future studies on the basis of a lower rate of toxic effects.

COMMENT BY MARK R. ALBERTINI, MD

Several studies have demonstrated limited benefits for chemotherapy for the treatment of patients with advanced non-small-cell lung cancer. These benefits

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include a modest improvement in overall survival as well as some improvement in overall quality of life. Several chemotherapy regimens are being used based on initial results suggesting potential benefit for several of these regimens. Thus, comprehensive phase III investigation was warranted to determine potential superiority of any of the newer chemotherapy regimens and to establish a reference regimen for subsequent clinical investigation. The study by Schiller et al provides comprehensive data on 1207 patients randomly assigned to receive 1 of 4 chemotherapy regimens for advanced non-small-cell lung cancer. They provide a comprehensive assessment of toxicity as well as clinical activity of each of these regimens. The toxicity with each of these regimens was particularly problematic in patients with a poor performance status. This toxicity resulted in a caution about the routine use of platinum-based chemotherapy for poor performance status patients. Schiller et al demonstrate no significant survival advantage for any of the 3 experimental regimens when compared with the reference regimen of cisplatin and paclitaxel. They identified less toxicity of carboplatin and paclitaxel when compared with the reference regimen of cisplatin and paclitaxel. Thus, carboplatin and paclitaxel was selected as a reference regimen for subsequent investigation. This selection was based on some improved toxicity profile, although improvement in survival was not achieved.

This phase III study clearly identifies the need for additional treatment approaches for patients with advanced non-small-cell lung cancer. The results achieved in this large number of prospectively randomized patients who were treated according to 1 of 4 regimens provide a valuable reference for subsequent studies. The limitations of current chemotherapy interventions are certainly highlighted by this report. Current chemotherapy regimens achieve only marginal benefit for patients with metastatic non-small-cell lung cancer. New approaches are required. Alternate treatments such as biologic response modifiers or interventions based on defined biologic targets may offer additional treatment opportunity.[5] Given the limited benefits with current chemotherapy approaches, participation in carefully designed clinical studies is required to make progress against this devastating disease. ❖

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Neoadjuvant Androgen Ablation Before Radical Prostatectomy in cT2bNXM0 Prostate Cancer

ABSTRACT & COMMENTARY

Synopsis: *Patients who are found to have positive surgical margins following radical prostatectomy have a much higher rate of disease progression than do patients with negative margins. The Lupron Depot Neoadjuvant Prostate Cancer Study Group recruited 303 patients with clinical stage T2b prostate cancer and randomized them to either 3 months of total androgen suppression followed by prostatectomy, or prostatectomy alone. This updated publication based on 5 years of follow-up reported that neoadjuvant hormones had no effect on recurrence rates despite significant pathological downstaging and, therefore, should not be recommended.*

Source: Soloway MS, et al. *J Urol*. 2002;167: 112-116.

The Lupron Depot Neoadjuvant Prostate Cancer Study Group conducted a trial from February 1992 through April 1994, and recruited 303 patients with clinical stage T2b disease who agreed to be randomized to surgery alone or hormonal pretreatment followed by prostatectomy. Patients were accrued at 27 institutions in the United States and Puerto Rico. The goal of the study was to determine whether pathologic downstaging would translate into better disease-free and overall survival. T2b patients were selected because a high percentage of them were typically upstaged to T3 at the time of surgery. All patients were < 75 years old and had a prostate-specific antigen (PSA) < 50 with negative bone scans and palpable disease consistent with stage T2b, ie, more than half of 1 lobe. Demographically, the 2 study groups were similar. The mean age in both groups was 65 years, and three quarters or more were white. The mean PSA in the neoadjuvant hormones arm was 14.3 (r, 0.6-50.3), and the mean PSA in the surgery alone group was 12.5 (r, 0.7-54.8). Total androgen suppression (TAS) therapy

consisted of 3 monthly injections of leuprolide along with flutamide 250 mg t.i.d. A fourth leuprolide injection was administered within 48 hours of surgery, but the rationale for the last shot was not mentioned.

There were 149 patients randomized to the neoadjuvant arm, of whom 138 were evaluable, and 154 randomized to the surgery alone arm, of whom 144 were evaluable. PSA levels were followed every 6 months for 5 years. PSA failure was defined as PSA > 0.4 ng/mL. There were 245 patients who underwent radical retropubic prostatectomy and 18 who underwent perineal procedures. The surgical approach in 12 patients was unknown. Nerve-sparing was attempted in 44% of the neoadjuvant hormones group and was successful in 89% of those. In the other group, it was attempted in 43% and was successful in 90% of those. A single pathologist at each institution was responsible for examining the surgical specimens, and all the pathologists met jointly on 2 occasions to discuss their findings. Specimens were sectioned at 2-mm intervals, and a positive margin required there to be ink on neoplastic cells.[1]

There were no significant differences in the numbers of patients in each group who were found to have seminal vesicle invasion (15% TAS group vs 22% surgery-alone group) or lymph node metastases (6% in both groups). The mean prostate volumes for the 2 groups did not vary significantly (35 cc TAS group vs 44 cc surgery alone group) nor did the mean Gleason score (6.7 TAS vs 6.4). There was a statistically significant improvement favoring the TAS group in capsular penetration (47% vs 78%; $P < .001$); positive urethral margin status (6% vs 17%; $P < .01$); positive surgical margin status (18% vs 48%; $P < .001$); and either positive surgical margin/lymph nodes/seminal vesicles (29% vs 57%; $P < .001$). Nevertheless, at 5-year follow-up, there was no difference in PSA recurrence rates for the 2 groups: 64.8% TAS patients and 67.6% surgery-alone patients had PSA relapses ($P = .66$). In the surgery alone group, 51.7% of the patients with positive margins relapsed, while 17.4% of the patients with negative margins relapsed ($P < .001$). In the TAS group, the percentages were 46.2% and 33% ($P = .31$). The only factor that was significantly related to margin status in logistical regression analysis was use of neoadjuvant hormones.

Soloway and associates concluded that there was no apparent adverse effect on the 5-year PSA relapse rate, but that hormonal pretreatment should generally be discouraged due to its cost and side effects.

COMMENT BY EDWARD J. KAPLAN, MD

Soloway et al found that downstaging their T2b patients did not confer a survival advantage. They postulated that cytologic alterations due to androgen deprivation may have made prostate cancer cells invisible to standard staining techniques, leading to false-negative margin reports. Unfortunately, since the study did not break out local recurrences vs. distant recurrences, we are left with the impression that surgical margins in downstaged glands are virtually prognostically irrelevant. This may or may not be the case. As a corollary in the radiation oncology literature, where hormones are used to cytoreduce large prostates prior to brachytherapy implants, Potters and colleagues reported a 5-year PSA relapse-free survival rate of 87% among 526 T1c-T2b brachytherapy patients treated with or without neoadjuvant androgen deprivation.[1] As a rule, since the radioactive seeds are placed < 5 mm beyond the prostate capsule, if downstaging does leave occult microscopic disease behind, then it would be hard to imagine that the control rates in the 2 groups of brachytherapy patients would be the same.

Soloway et al settled on 3 months of neoadjuvant hormones because it was not too short and not too long. It is unclear why a fourth shot was given just prior to surgery. A broad range of patients was included in the trial, some with high PSAs, and others with low PSAs. PSA is well recognized as the most important prognostic factor in prostate cancer, so perhaps neoadjuvant hormones might benefit only those patients in an intermediate PSA risk group, such as patients whose PSAs are 10-20. It is certainly conceivable that patients with high PSAs would not be expected to benefit from downstaging of local disease because of the high likelihood of occult metastatic disease. Soloway et al only reported mean PSAs, so it is unclear how many patients actually had PSAs > 20.

At the discretion of the surgeon, nerve-sparing could be attempted. It is unclear whether this may have had an effect on margin status. We are also not told whether some centers were more successful than others in achieving negative margins, or how many patients each center contributed.

Soloway et al stated that "the PSA level that indicates biochemical failure and progression after radical prostatectomy is uncertain. We used a cut-off of 0.4 ng/mL." To support this notion, he cited an article by Amling and associates that explored the most appropriate cut point.[3] In his review of 2782 men with clinical stage T1-2 cancer who underwent radical prostatectomy, Amling et al reported that the 5-year biochemical, ie, PSA, progression-free percentages for cut points 0.2, 0.3, 0.4, and > 0.5 ng/mL were 62%, 72%, 76%, and 78%. Amling et al suggested that PSA > 0.4 ng/mL might be the most

appropriate cut point "since a significant number of patients with lower PSA do not have a continued increase in it." Many clinicians would take issue with the argument that a PSA at or below a point where "only 28-38% of patients" progress should be used as a benchmark for success. While 0.4 ng/mL might be useful for patients treated with radiotherapy, it seems too high when talking about prostatectomy patients. No data are provided regarding how many patients maintained a PSA of zero during the study period.

This study was an interesting step in evaluating the use of neoadjuvant hormones preceding radical prostatectomy. Soloway et al are looking forward to publication of the Canadian Urologic Oncology Group trial results, in which 3 vs. 8 months of androgen deprivation are being assessed.[4] ❖

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Surgical Staging and Neoadjuvant Therapy in Esophageal Cancer

ABSTRACT & COMMENTARY

Synopsis: *Forty-five surgically staged patients with esophageal cancer who received preoperative chemoradiotherapy were studied. Although pretreatment nodal status predicted response to therapy, the post-treatment pathologic findings were correlated with survival. The entire group had a 3-year survival of 34%. There were no 2-year survivors if the post-treatment lymph nodes had residual cancer.*

Source: Suntharalingam M, et al. *Cancer J*. 2001;7:509-515.

Suntharalingam and associates present a large series with long-term follow-up of patients with surgically staged esophageal cancer who were treated with chemoradiotherapy (CRT) followed by definitive surgery. Forty-five patients were identified retrospectively who had undergone pretreatment surgical staging (PTSS) with a thoracoscopy and/or laparoscopy. The thoracoscopy included routine biopsies of regional nodes, and the esophagus was inspected for localized extension, which would be deemed unresectable. Laparoscopy included sampling of regional nodes and inspection of the liver. There were 15 node-negative and 30 node-positive patients.

Chemotherapy consisted of 2 4-week cycles of 5-FU (1000 mg/m^2/d for 96 hours) and cisplatin (100 mg/m^2, day 1). Concurrent radiation was delivered to the primary tumor and only those nodal areas proven to be involved by pathologic staging. The treatment delivered 39.6 Gy at 1.8 Gy per fraction, followed by a 10.8 Gy boost to the gross tumor volume. With just 2 exceptions, surgery was performed via a transthoracic approach (Ivor-Lewis esophagectomy) that included complete regional lymph node dissection.

The pretreatment nodal status was the only significant predictor of response to CRT. For example, a pathologic complete response (pCR) was found in 59% of node-negative patients (sterilized tumor bed) and 14% of node-positive patients (sterilized tumor bed *and* nodes). No difference between squamous cell carcinoma and adenocarcinoma emerged.

The 15 node-negative patients had the best median survival of 35 months. Sixty-eight percent of node-positive patients had no evidence of nodal disease after CRT resulting in a median survival of 17 months (with a 40% survival at 3 years). Unfortunately, the remaining node-positive patients with residual microscopic nodal involvement had a median survival of 5 months (with no 2-year survivors). Therefore, the most important predictor of survival turned out to be the nodal status at the time of esophagectomy.

COMMENT BY KENNETH W. KOTZ, MD

There have been at least 46 nonrandomized and 6 randomized trials of preoperative CRT in esophageal cancer.[1] Three of the 6 randomized trials showed a benefit in either overall or disease-free survival.[1,2] Despite provocative data, as discussed by Dr. Morris in the November 2001 issue of *Clinical Oncology Alert*,[3] the definitive study proving superiority of any approach over surgery alone in esophageal cancer has not been performed.

The study by Suntharalingam et al is interesting because all patients were staged surgically. However, because "the vast majority of node-positive patients were discovered laparoscopically" (data not provided), the node-positive patients in this study might represent a population with a different prognosis than other series in which node-positive patients were detected radiographically. Furthermore, because initial esophagectomy was not performed, the false-negative rate associated with PTSS is undetermined.

Unfortunately, even though all patients were also staged with CAT scans, EGD with ultrasound, and where indicated, MRI and bronchoscopy, Suntharalingam et al do not report either the correlation with the PTSS or the radiographic response rate.

One of the important conclusions by Suntharalingam et al is that "trimodality therapy offers patients with esophageal cancer an opportunity for long-term survival." Although lymph node status was the strongest predictor of survival, it is not reported whether node-positive patients with a pCR fared better than those patients who, after CRT, had negative nodes but persistent disease in the esophagus. Nevertheless, their conclusion is supported by a 3-year survival of 34% for the entire study group. On the other hand, the subgroup with persistent nodal involvement had no 2-year survivors. Although the numbers are small, Suntharalingam et al state "one could make a strong argument" to abort the esophagectomy if persistent nodal disease is discovered.

Another conclusion reached by Suntharalingam et al is that "pretreatment surgical staging provides useful information that can help in the selection of appropriate patients for aggressive therapy." For example, the PTSS was used to tailor the design of the radiation fields. While it seemed reasonable to cover only the pathologically involved nodal regions, there is no evidence that this is superior to standard empirically derived radiation fields or that it ultimately results in less toxicity. In addition, although termed "minimally invasive surgical staging," all patients required chest tubes and an average 3-day hospital stay with 1 pneumothorax requiring a prolonged chest tube.

Did the PTSS really help in selecting patients for trimodality therapy? The 45 patients identified for this study came from a cohort of 72 patients considered for trimodality therapy. Only 2 of these 72 patients were found to be unresectable based on PTSS, both having radiographically undetectable liver metastases. Inoperable esophageal cancer patients can also be identified by PET scans[4], which have been shown to correlate with response to therapy as well as survival.[4,5] In fact, PTSS does not seem to affect decision making. First, PTSS does not identify a subset of patients in whom preoperative CRT is either required or can be avoided. Second, the post-treatment pathologic findings seem to be most predictive of prognosis.

The role of neoadjuvant therapy in esophageal cancer remains controversial. It has been reported that a positive biopsy, in the absence of an endoscopically visible lesion, almost always corresponds to an intramucosal tumor without nodal metastases.[6] These patients may be best served by a vagal-sparing or simple transhiatal esophagectomy[6] and thus may not require CRT. On the other hand, operable candidates whose tumors are not technically resectable may benefit from the downstaging that occurs with preoperative CRT.[2] For all others, preoperative CRT followed by esophagectomy is an option for medically fit patients, although esophagectomy alone must be presented as a treatment choice. ❖

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Cytokeratin 20 in Noncolorectal Lymph Nodes

ABSTRACT & COMMENTARY

Synopsis: *Cytokeratin 20 (CK20) is a member of the intermediate filament protein family that has been studied as a specific marker for disseminated colorectal cancer cells. The specificity of CK20 was examined by a real-time PCR assay to determine CK20 expression in tumors and lymph nodes of subjects with colorectal and breast cancer, head and neck and vulvar squamous cell carcinoma, and melanoma. Low-level CK expression was detected in infiltrated lymph nodes from subjects with noncolorectal cancer types and suggest potential advantage of detecting circulating epithelial cells by quantitative PCR.*

Source: Soong R, et al. *Clin Cancer Res*. 2001;7: 3423-3429.

Cytokeratin 20 (CK20) is a keratin protein with known distribution in epithelial cells of the gastrointestinal tract.[1] Immunohistochemical studies have suggested potential use of CK20 as a means to separate adenocarcinomas of gastrointestinal vs. nongastrointestinal origin.[1] However, more sensitive assays such as

a CK20-reverse transcription (RT)-PCR assay, have reported positivity in several other types of cancer cells, including breast cancer cells.[2] The CK20-RT-PCR assay has been used to detect disseminated colorectal cancer cells in lymph nodes, blood, and bone marrow and has been suggested to represent a means to significantly improve current staging protocols for colorectal cancer patients.[3] The CK20-RT-PCR assay was used in combination with a CEA-RT-PCR assay to enhance ability to detect circulating tumor cells in a study involving 100 colorectal cancer patients (50 primary tumors only and 50 liver metastases) and 70 control individuals without known cancer.[4] Circulating colorectal cancer cell positivity was detected in 48% of colorectal cancer patients with 1 sample of CEA alone, 34% with 1 sample of CK20 alone, and 74% when both assays and 3 samples were used to identify circulating cancer cells.[4] However, 3 noncancer patients (4.3%) were positive for either CEA (2 patients) or CK20 (1 patient). It was suggested that RT-PCR-based studies for circulating cancer cells should involve multiple blood samples with identification of multiple tumor related cDNA products.[4] Thus, additional study to determine the specificity and reproducibility of CK20 assays was needed.

This study by Soong and colleagues used 4 methods for RT-PCR quantification to clarify the expression profile and specificity of CK20 expression. Samples were obtained from 10 colorectal tumors and 11 breast tumors as well as 98 lymph nodes from various cancer types from subjects undergoing surgery for their disease. RT-PCR reactions were performed for CK20 and for the housekeeping gene, porphorynbilinogen deaminase (PBGD). Rigorous optimization experiments with the HT29 colon carcinoma call line and the HL60 promyelocytic leukemia cell line were performed to demonstrate sensitivity and specificity of these assays. CK20 could be detected in a dilution of 10 HT29 cells mixed with 1,000,000 HL60 cells, while no signal was detected from 1,000,000 HL60 cells alone. The reproducibility of each of the 4 methods for quantifying CK20 was assessed using a single tissue sample in a total of 27 replicates for each method, involving 3 serial dilutions, 3 separate reverse transcriptions, and 9 individual PCR assays. The coefficient of variation for each of the 4 methods was 43%, 32%, 12%, and 13%. Of the tumors evaluated, 10 of 10 (100%) of the colorectal cancers and 8 of 11 (73%) of the breast cancers were CK20 positive. Of the lymph nodes evaluated, 9 of 9 (100%) of the colorectal lymph nodes and 41 of 89 (46%) of the noncolorectal lymph nodes had detectable CK20 mRNA. A strong correlation existed between CK20 detection and lymph node epithelial invasion in the noncolorectal lymph nodes. The CK20 quantity, as assessed by the mean relative CK20 quantity, was significantly higher in colorectal than noncolorectal samples. Soong et al concluded that a standardizable, quantitative CK20 PCR assay can be used to characterize epithelial-specific, low-level CK20 expression in cancer types not expected to express CK20. The clinical implications of these findings require further analysis.

COMMENT BY MARK R. ALBERTINI, MD

The use of monitoring tools, such as detection of CK20 in blood, lymph node, or tumor samples, represent potential surrogate markers for biological activity of several cancers. Soong et al describe several essential issues that need to be addressed when evaluating a potential surrogate marker for cancer. The assay needs to be quantitative and needs to be reproducible. The assay should ideally use a small amount of clinical material and have some correlation with biological activity of the cancer. The assay should be reflective of the in vivo situation and require minimal in vitro manipulations. The assay should have some reference standard for purposes of comparison. The current report's description of the characterization and evaluation of sensitivity and specificity of the CK20 RT-PCR assays fulfills many of these criteria. The evaluation of a biological assay requires some understanding of the assay accuracy, precision, specificity, and sensitivity. This careful description of assay standardization should be required of all reports describing potential surrogate markers.

The current report clearly identifies low-level, epithelial cell-specific CK20 expression in infiltrated lymph nodes from subjects with noncolorectal cancers. The discrepancies in prior reports likely resulted from variability in the sensitivity of the assays used for CK20 detection. While the level of CK20 expression appears to be much greater in colorectal samples, low-level expression was also present in noncolorectal samples. Thus, a reproducible assay exists and the biological relevance of CK expression in tumors, lymph nodes, and blood can now be addressed for several tumor types in larger prospective clinical studies. A careful description of CK20 assay characteristics will be an essential requirement for meaningful testing of this potential surrogate marker in clinical studies. ❖

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CME Questions

7. Which of the following statements is true about chemotherapy regimens for advanced non-small-cell lung cancer patients?

a. The regimen of carboplatin and paclitaxel has more Grade 4 and 5 toxicity compared with cisplatin and paclitaxel.
b. The regimen of cisplatin and gemcitabine has improved survival compared with cisplatin and paclitaxel.
c. The regimen of cisplatin and docetaxel has improved 1-year survival compared with cisplatin and paclitaxel.
d. Patients with a performance status of 2 appear more likely to have significant adverse events with platinum-based combination chemotherapy.

8. Which of the following statements best describes the pathologic findings noted in the neoadjuvant lupron/flutamide prostatectomy study?

a. There were more patients in the surgery-only arm with metastatic disease in their lymph nodes than there were in the TAS arm.
b. There were more patients in the surgery-only arm with seminal vesicle invasion than there were in the TAS arm.
c. There were more patients in the surgery-only arm with positive surgical margins than there were in the TAS arm.
d. There were more patients in the surgery-only arm with positive bone scans than there were in the TAS arm.

9. Which of the following statements is *false* regarding the neoadjuvant hormones prostastectomy trial?

a. Patients treated with surgery alone had the highest positive surgical margin rate.
b. Patients treated with surgery alone who had positive surgical margins had the highest PSA recurrence rate.
c. Patients treated with neoadjuvant hormones who had negative surgical margins had the lowest PSA recurrence rate.
d. Patients treated with neoadjuvant hormones had the lowest positive surgical margin rate.

10. In the study of surgical staging and preoperative chemoradiotherapy, which of the following is true?

a. Survival was correlated with the pathologic findings at the time of esophagectomy.
b. Survival after chemoradiotherapy was equivalent whether surgery was performed.
c. Survival was correlated with the dose intensity of the chemotherapy.
d. Surgical mortality was unacceptably high after chemoradiotherapy.

Readers are Invited. . .

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