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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

New Therapeutic Modalities In Testing For Patients With Carcinoid Syndrome

By Lawrence M. Prescott

While octreotide acetate (Sandostatin, Novartis), the original long-acting somatostatin analogue approved in 1988, still continues to be a mainstay in the medical management of the signs and symptoms of carcinoid syndrome, a number of new therapeutic modalities, the newest of which are radio-labelled formulations being developed for both diagnosis and treatment, offer hope for patients with this disease, according to Larry Kvols, speaking at the California Carcinoid Fighters Seminar.

The original octreotide preparation recently was formulated into a

(Continued to page 2)

Patient Care:

Nurses' Work Environment Needs Change To Protect Patients From Errors, IOM Says

The work environment of nurses, the largest segment of the nation's health care work force, needs to be substantially transformed to better protect patients from health care errors, says a new report from the Institute of Medicine of the National Academies.

The report calls for changes in how nurse staffing levels are established and mandatory limits on nurses' work hours as part of a comprehensive plan to reduce problems that threaten patient safety by strengthening the work environment in four areas: management, work-force deployment, work design, and organizational culture.

"No one or two actions by themselves can keep patients safe," said Donald Steinwachs, chairman of the committee that wrote the report, and chairman of the department of health policy and management, Bloomberg School of Public Health, Johns Hopkins University. "Rather, creating work environments that reduce errors and increase patient safety will require fundamental changes in how nurses work, how they are deployed, and how the very culture of the organization understands and acts on safety. We present a comprehensive plan to address all these areas."

The nation's 2.2 million registered nurses, 700,000 licensed practical and vocational nurses, and 2.3 million nursing assistants constitute 54 percent of all health care providers. Nurses are the health professionals who interact most frequently with patients in all settings, and their actions—such as ongoing monitoring of patients' health status—are directly related to better patient outcomes. Studies show that increased infections,

(Continued to page 3)

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New Approaches Tested For Carcinoid Syndrome

(Continued from page 1)

long-acting once-a-month octreotide injection (Sandostatin LAR Depot, Novartis) which has been proven to be just as effective as the three-times daily self injection of standard octreotide, simplifying management of the symptoms of carcinoid syndrome, said Kvols, professor of medicine and interdisciplinary oncology, H. Lee Moffitt Cancer Center & Research Institute, University of South Florida.

In addition, octreotide now is being used as the building block for a number of radio-labelled formulations useful both in diagnosis and treatment of carcinoid syndrome. The first of these is ^{111}Indium DTPA-octreotide (Octreoscan, Mallinckrodt Medical). When administered in low doses, this agent can be used as a diagnostic tool, giving off gamma radiation which is picked up by tumors with somatostatin receptors and is detectable with appropriate gamma camera imaging technology.

At higher doses, a number of the new radio-labelled formulations show considerable promise as radiotherapeutic agents for the targeted therapy of carcinoid syndrome, Kvols said. These include high dose Octreoscan, also known as ^{111}In-DPTA-Octreotide or ^{111}In-penetatreotide (SomatoTher, LSU Medical Center Foundation), and ^{90}Yttrium-DOTA-octreotide (OctreoTher, Novartis). These agents have a double-barrelled capacity, with the radiation slowing down vessel growth and the octreotide suppressing hormonal actions.

In a dose-ranging study of ^{111}In-pentatreotide, Kvols said, 85 patients received the radiolabelled formulation at 500 to 600 milliCuries once, twice or four times. Overall, the partial response was 8%, with 70% of patients having stable disease. In comparable studies with sandostatin, the partial response has been reported to be with 2% stable disease being 45%, while ultrahigh dose sandostatin treatment produces a partial response rate of 7%, with 47% of patients having stable disease.

The ^{90}Y-DOTA-octreotide compound, unlike the ^{111}In-DPTA-octreotide formulation, is a beta emitter, so it cannot be seen with the gamma camera, Kvols said. Uptake of the radioactive material can be seen with PET studies of the kidney, liver, and bladder, however, the radioactive material being more evident in patients with carcinoid syndrome. Most recently, a phase II dose-escalating trial has been completed at three centers—the University of South Florida at Tampa, Erasmus University in Rotterdam, The Netherlands, and Catholic University of Leuven, Belgium and the data is presently under consideration at the FDA. The study enrolled 60 patients, three per dose cohort, with each cohort getting progressively higher doses. Thirty-five of the patients had carcinoid syndrome and 25 had eyelet cell cancers of the pancreas. In this latter group, 8 patients had functioning tumors, 10 had non-functioning tumors, and 5 were unclassified.

Overall, Kvols said, the drug was well tolerated with a remarkable safety profile. Some patients showed a 20% decrease in kidney function, but no need for dialysis; there was some mild anemia, treatable with erythropoietin; some leukopenia, which was easily reversible; some reversible impairment in sperm production; and no diabetes mellitus.

A total of 52 of the 60 patients received the maximum allowable dose, with 18 of the 52 already symptom-free when they entered the trial, Kvols said. A total of 41 of the 52 patients had stable disease when they went on therapy and of these patients, eight patients had stable disease under prior octreotide treatment.

At the end of the study, there were 5 partial responses and 7 minor responses for an overall response rate of 24%. Thirty patients had stable disease, including the eight patients who had stable disease under prior octreotide treatment. Overall,

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there was a 10% partial response, 50% stable disease, 27% of patients showed progression of disease, and the remainder were minor responses or indeterminant. Sixty-five percent of the patients had improvement according to the Southwest Oncology Group status.

Time to first progression in stable patients was 42 months, while in those who were progressing at the start of treatment, time to first progression after treatment was 30 months, Kvols said. In the 60 patients in this study, median survival had not been reached at 59 months, with more than 50% still alive. In contrast, in the 85 patients who received the high dose ^{111}In-DOTA-octreotide formulation, median survival was 22 months.

Patient Care:

IOM Report: Nursing Workplace Needs Substantial Change

(Continued from page 1)

bleeding, and cardiac and respiratory failure are associated with inadequate numbers of nurses. Nurses also defend against medical errors. A study in two hospitals found that nurses intercepted 86 percent of medication errors before they reached patients.

Despite the growing body of evidence that better nursing staff levels result in safer patient care, nurses in some health care facilities may be overburdened. Some hospital nurses may be assigned up to 12 patients per shift. Available methods for achieving safer staffing levels—such as authorizing nursing staff to halt admissions to their units when staffing is inadequate for safe patient care—are not employed uniformly by either hospitals or nursing homes.

The decade-old regulations that specify minimum standards for staffing in nursing homes need to be updated, the report says. The U.S. Department of Health and Human Services should require nursing homes to have at least one RN within the facility at all times. HHS also should specify staffing levels that increase as the number of patients increases and that are based on the department's 2001 report to Congress on minimum staff-to-patient ratios for nursing homes. The committee recommended that nursing homes increase internal oversight of their staffing practices and effects on patient safety whenever staffing falls below one RN for every 32 residents, one licensed nurse per 18 residents, and one nurse assistant per 8.5 residents per day. Similarly, hospital intensive care units should increase internal oversight when staffing falls below one nurse for every two ICU patients. Federal and state report cards on nursing homes should include information on nursing staff levels, and measures of staffing levels should be developed for hospital report cards. Whenever possible, health care facilities should avoid using nurses from temporary agencies to fill staffing shortages.

Long work hours pose one of the most serious threats to patient safety, because fatigue slows reaction time, decreases energy, diminishes attention to detail, and otherwise contributes to errors. While most nurses typically work eight- to 12-hour shifts, some work even longer hours. At the same time, patients admitted to hospitals typically are more acutely ill and require technologically more complicated care than in the past. State regulatory bodies should prohibit nursing staff from working longer than 12 hours a day and more than 60 hours per week, the committee said.

Along with changes in staff levels and hours, hospital restructuring initiatives begun in the mid-1980s led to substantial changes in how nurses work. As hospitals tried to respond to the financial pressures resulting from modifications to public and private insurance payment systems, their efforts altered the ways in which nurses are organized to provide care and, in many cases, undermined trust between nurses and management. As a key step toward improving nurses' work environments and restoring trust, the report urges health care organizations to involve nurse leaders in all levels of management and to solicit input from nursing staff on decisions about work design and implementation. Nurses are in prime positions to help pinpoint inefficient work processes that could contribute to errors, identify causes of nursing staff turnover, and determine appropriate staff levels for each unit.

Orientation programs for newly hired nurses and continuing education programs are being scaled back due to cost pressures, although surveys indicate that many newly licensed nurses do not possess the overall preparation to provide care to today's patient population. Also, many RNs are not receiving ongoing education and training to keep up with the ongoing growth of new medical knowledge and technology. Health care organizations should dedicate financial resources to support nursing staff in the ongoing acquisition and maintenance of knowledge and skills, the report says.

The committee's recommendations are made in

a climate of high rates of turnover among nursing staffs, as well as a nursing shortage that is predicted to worsen in the future. Implementation of the recommended changes in nurses' work environments would likely help health care organizations recruit and retain nurses, the report says.

"It may be tempting to think that these recommendations can wait for increases in the supply of nurses, but evidence on nursing retention indicates just the reverse is true," Steinwachs said. "Because the supply of nurses is unfortunately stretched thin right now, they must be supported by work processes, work spaces, hours, staffing practices, and a culture that better defends against errors and readily detects and mitigates errors when they occur. Nurses will be more likely to stay in health care organizations that implement the management and work-design practices recommended in this report."

The study was sponsored by the U.S. Department of Health and Human Services' Agency for Healthcare Research and Quality.

Copies of the report, "Keeping Patients Safe: Transforming the Work Environment of Nurses," are available at www.nap.edu. Copies of the report will be available early next year from the National Academies Press; tel. 202-334-3313 or 800-624-6242.

Prostate Cancer:

High Radiation Dose Effective Ten Years After Treatment

Men with clinically localized prostate cancer, treated to high dose levels with three-dimensional conformal radiation therapy, achieved long-term PSA relapse-free survival with minimal side effects, according to a study presented at the annual meeting of the American Society for Therapeutic Radiology and Oncology in Salt Lake City last month.

Researchers from Memorial Sloan-Kettering Cancer Center presented findings from the 10-year retrospective study.

"This is the first study that is looking at 10-year results of dose escalation with 3D-CRT and demonstrating improved outcomes in all subgroups of patients treated with high doses of radiation compared to lower conventional dose levels," said the study's lead author Michael Zelefsky, chief of MSKCC's Brachytherapy Service. "We observed that the radiation dose was one of the critical ingredients, or predictors, for achieving improved outcome and enhanced disease control rates in each of the patient groups we evaluated."

Researchers analyzed data from 828 MSKCC patients treated between 1988 and 1997. The patients were categorized into prognostic risk groups based on pre-treatment PSA levels, Gleason score, and clinical stage. At 10 years, the PSA relapse-free survival (PRFS) outcomes for favorable, intermediate, and unfavorable risk patients were 70 percent, 49 percent, and 35 percent respectively. Higher radiation dose levels (the doses in the study ranged from 64.8 Gy up to 75.6 Gy) were associated with an improved PRFS at 10 years for each prognostic group.

The other significant finding of the study is that patients had minimal side effects, despite the fact that higher doses of radiation were delivered. The long-term risk of serious rectal or bladder injuries at 10 years was 2 ½ percent and 1 ½ percent, respectively.

"This dispels the notion that as time goes on the side effects become more noticeable and patients are more at risk for developing long-term damage years out from treatment," Zelefsky said.

"Radiation dose has a significant impact on the outcome of patients with localized prostate cancer treated with radiation therapy," said Steven Leibel, chairman of MSKCC's Department of Radiation Oncology and the study's senior author. "We continue to observe that even higher doses have further improved cure rates for patients with localized prostate cancer. These mature data show that even 10 years from the therapy, despite the application of high radiation doses, the tolerance was excellent."

New Risk Stratification Method For Prostate Cancer Described

A new study finds changing where on the prostate gland a surgeon takes a biopsy may improve prediction of whether a patient's treatment is successful.

The study is scheduled for publication in the Dec. 1 issue of CANCER and was published online last month at www.interscience.wiley.com/cancer.

After diagnosis of prostate cancer, physicians commonly use prostate surface antigen level and tumor grade and clinical stage of disease to determine a patient's prognosis. Recently, research has begun to focus on using estimates of tumor cells gathered by prostate needle biopsies (PNBx) to create a more useful model to determine treatment outcome.

To do PNBx, surgeons take sample cores from

both halves, or "lobes" of the prostate. A core is "positive" if it contains cancer. Previously, researches found that the total percentage of cancer-positive cores from the entire prostate was useful to predict treatment failure. However, scientists observed another trend - that patients with evenly distributed disease to both lobes had a lower risk of treatment failure than patients with a similar burden of disease only in one lobe.

Researchers led by Stephen Freedland, of the Department of Urology at the University of California, Los Angeles, investigated whether which was a better outcome predictor for patients who had undergone surgery to remove the prostate: the percent of positive cores from both lobes or from the most affected or "dominant" lobe.

They found the percent of positive cores from the dominant side was a better predictor of treatment failure within two years than either the percent of positive cores for the entire prostate or the percent of positive cores from the non-dominant lobe. Patients could then be stratified according to the percent of positive cores from the dominant side: low risk (<34 percent), intermediate risk (34-67 percent), and high risk (>67 percent). When combined with PSA level and tumor grade, the percent of positive cores from the dominant side of the prostate strongly predicted treatment failure within two years.

"Adverse pathology and PSA failure are largely determined by the dominant tumor bulk, as reflected by the percentage of cores positive from the dominant side," conclude the authors.

Ovarian Cancer:
Doxil/Caelyx Survival 3 Weeks Longer Than Topotecan

Researchers presented updated data comparing Doxil/Caelyx (doxorubicin HCI liposome injection) to topotecan HCI in patients with recurrent ovarian cancer. The data, from randomized, controlled, multi-center, open-label, phase III study, were presented during a poster session at the 12th meeting of the Federation of European Cancer Societies in Copenhagen, Denmark.

The analysis compared Doxil and topotecan in ovarian cancer patients whose disease recurred after or did not respond to first-line platinum-based chemotherapy. The primary objective of the long-term follow-up analysis was to measure the overall survival and progression-free survival of the patients.

Median overall survival was three weeks longer for patients treated with Doxil compared to those treated with topotecan (63 and 60 weeks, respectively, HR 0.82 [95 percent CI=0.68 to 1.00]; p=0.05. In addition, the overall progression-free survival was 16.1 weeks for Doxil compared to 17.0 weeks for topotecan (HR 0.88 [95 percent CI=0.73 to 1.06]; p=0.171).

Among platinum-sensitive patients (those who had a PFS interval of greater than six months after first-line, platinum-based chemotherapy), the median survival of patients receiving Doxil was 112 weeks versus 77 weeks for patients receiving topotecan (HR 0.63 [95 percent CI=0.47 to 0.85]; p=0.002. Doxil patients also saw a significant advantage in median PFS versus those receiving topotecan (28.9 and 23.1 weeks, respectively, HR=0.76 [95 percent CI=0.58 to 1.00];p=0.046.

In the subset of patients with platinum-refractory disease, median survival was similar in the two treatment groups (36 weeks for Doxil and 41 weeks for topotecan, HR=1.01 [95 percent CI=0.78 to 1.31];p=0.943), as was PFS (median 9.4 ad 13.6 weeks respectively, HR=1.00 [95 percent CI=0.77 to 1.29];p=0.983).

"These updated results provide important information in terms of future research directions and treatment options in recurrent epithelial ovarian cancer," said Alan Gordon, director of research in gynecology for US Oncology, and lead author of the study.

A total of 474 patients were randomly assigned to receive either Doxil 50 mg/m^2 every 28 days (up to six cycles). A total of 239 patients received Doxil; 235 patients received topotecan. This analysis was performed after 90 percent of the subjects either had died or were lost to follow-up.

No signs of congestive heart failure were reported in either treatment group. Severe hematologic toxicities for Doxil and topotecan, respectively, included neutropenia, 35 percent vs. 81 percent; anemia, 35 percent vs. 72 percent; thrombocytopenia, 13 percent vs. 65 percent; and leukopenia, 36 percent vs. 64 percent.

Alopecia was reported in 16 percent of Doxil-treated patients and in 49 percent of those receiving topotecan. Hand-foot syndrome was reported in 49 percent of Doxil-treated patients and in one percent of topotecan-treated patients. The incidence of stomatitis was 40 percent for Doxil and 15 percent for topotecan.

Liver Cancer:

Survival After Liver Transplant Called Excellent In Study

In the first national study to examine survival among liver transplant patients with advanced hepatocellular carcinoma, researchers found excellent five-year survival results, with a steady improvement over the last decade.

Results of the study will be published in the Journal of Clinical Oncology.

Most patients with hepatocellular carcinoma (HCC), also known as hepatoma, have cirrhosis, a risk factor of hepatoma, and are inoperable because of tumor size, location or severity of underlying liver disease.

"This study shows that we can achieve excellent survival with liver transplantation among patients with hepatoma, confirming similar results reported by single center studies," said Paul Thuluvath, senior author and associate professor in the Department of Medicine at Johns Hopkins University School of Medicine. "These findings are particularly reassuring for patients with tumors that cannot be surgically removed, which comprise more than 80 percent of HCC patients."

The primary objective of the study was to determine survival in an unselected patient population who had liver transplantation for HCC. Using the United Network for Organ Sharing database, researchers collected data on 48,887 patients who underwent liver transplantation in the United States between 1987 and 2001. Patients were excluded if they had undergone multiple organ transplantation, retransplantation, were less than 18 years of age, or lacked survival information.

Of the remaining patients included in the final analysis, 985 had liver transplantation for hepatocellular carcinoma (hepatoma group) and 33,339 patients had liver transplantation for other reasons (control group). Both the hepatoma and control groups were divided into three different five-year time periods: 1987-1991, 1992-1996, and 1997-2001.

Researchers found significant and steady improvement in survival over time among liver transplant patients with HCC, particularly in the last five years. Five-year survival improved from 25.3 percent during 1987-1991 to 47 percent during 1992-1996, and 61.1 percent during 1996-2001.

"Although the survival is low in patients with hepatoma as compared to patients who had transplantation for non-malignant liver conditions, excellent five-year survival rates in patients with HCC suggest that liver transplantation is the treatment of choice in patients with advanced cirrhosis and HCC," said Thuluvath.

Researchers also wanted to see whether the Milan criteria for selecting HCC patients for liver transplantation, incorporated by many transplant centers as a guideline after a landmark study in 1996, had any indirect effect on patient survival among the 1997-2001 group. Milan criteria require that tumors be less than five centimeters, less than three centimeters if there are one to three tumors, and no invasion of blood vessels or lymph nodes.

Study authors noted that the excellent survival results between 1997 and 2001 may be a result of careful patient selection based on the improved Milan criteria, but cautioned that this finding is based on speculation.

Researchers also noted several limitations to the study. Because they examined a large database and did not have information on detailed staging of individual patients and the actual criteria used at the time of liver transplant, critical information about how patients were selected, tumor size and histology, and the extent of a patient's liver disease remains unknown.

Also, given the prevalence of hepatoma worldwide and the limited supply of organs, researchers pointed to the need for better surveillance, detection and prevention of hepatoma and underlying cirrhosis, and universal HBV vaccination, particularly for countries where organ transplantation is not always an option.

Lung Cancer:

Tumor Size Predicts Survival In Early-Stage Lung Cancer

Tumor size is an important predictor of survival in patients with early-stage lung cancer, says a study published in the November issue of CHEST, the peer-reviewed journal of the American College of Chest Physicians.

The study shows that patients with lung tumors less than 2 cm in size had a higher 5-year survival rate than patients with tumors 2 to 3 cm in size. The study also suggests that despite current lung cancer staging guidelines, which categorize lung tumors as being less than, equal to, or more than the baseline

value of 3 cm, further substaging may be needed to accurately assess and treat the disease.

"Although previous studies have noted a distinct difference in survival between patients with nonmetastasized tumors less than 3 cm [stage IA] and tumors more than 3 cm in size [stage IB], little information is available on whether size remains an important determinant of survival in tumors less than 3 cm," said Jeffrey Port, assistant professor of cardiothoracic surgery, Department of Cardiothoracic Surgery, Weill-Cornell Medical Center. "Our study indicates that within stage IA, a tumor size difference of even 1 cm can impact survival, leading us to believe that further substaging of stage IA lung cancer is necessary to ensure patients in this stage are receiving the most effective treatment."

Researchers reviewed the history of 244 patients who underwent surgical resection for lung tumors. Overall mortality/survival rates and mortality/survival rates specific to lung cancer were analyzed and compared to tumor size. The overall 5-year survival rate was 71.1 percent, as compared to the overall 5-year disease-specific survival rate of 74.9 percent.

In regard to tumor size, disease-specific survival was 81.4 percent for patients with tumors less than or equal to 2 cm and 63.4 percent for patients with tumors greater than 2 cm.

Breast Cancer:

B-27 Finds Improved CR For Taxotere Prior To Surgery

Study results published Journal of Clinical Oncology may provide support for the early use of Taxotere (docetaxel) in the treatment of breast cancer.

The study, conducted by the National Surgical Adjuvant Breast and Bowel Project, showed improved clinical and pathological complete response rates in patients with operable breast cancer who were given Taxotere in addition to a standard anthracycline-based regimen prior to surgery, compared with those patients who only received the pre-operative (neoadjuvant) anthracycline-based regimen.

"While we've known for some time that neoadjuvant chemotherapy is beneficial for patients with more advanced breast cancer, this study demonstrates that patients with less advanced or operable breast cancer may also benefit from this approach," said lead investigator Harry Bear, professor and chairman, Division of Surgical Oncology, Virginia Commonwealth University's Medical College of Virginia and the Massey Cancer Center. "The addition of Taxotere to the pre-operative regimen significantly improved response rates. Research shows that improvement in response rates are predictive of longer survival for patients, which is why we are so encouraged by these results."

In the phase III study (NSABP Protocol B-27) patients were randomized to receive either four cycles of doxorubicin and cyclophosphamide (AC) followed by surgery (Group I) or four cycles of AC followed by four cycles of Taxotere, followed by surgery (Group II) or four cycles of AC followed by surgery and then four cycles of Taxotere (Group III). Among the most compelling findings was a 91 percent increase in pathologic complete response rate among patients in Group II (AC followed by Taxotere), compared with those patients given just AC (26.1 percent vs. 13.7 percent).

In addition to the statistically significant increase in pathologic complete response, patients in Group II (AC followed by T) also experienced a higher clinical complete response rate than patients given AC alone (63.6 percent vs. 40.1 percent) and a higher overall response rate or tumor shrinkage (90.7 percent vs. 85.5 percent). There was also an improvement in nodal status among patients given Taxotere as part of the neoadjuvant regimen compared with those given AC alone (58.2 percent pathologically node-negative vs. 50.8 percent).

In the study, 10.3 percent of patients experienced a grade 4 toxicity while receiving AC, and 23.4 percent of patients experienced a grade 4 toxicity while receiving Taxotere. The most common grade 4 event experienced by patients during treatment with Taxotere was febrile neutropenia (21.2 percent).

Brain Tumors:

Studies Link Age-Dependent Outcome To Immune Cells

Chronological age at time of diagnosis has long been associated with a patient's prognosis and length of survival in the battle against brain tumors and other cancers. Older patients typically respond less favorably to treatment and have comparatively poorer outcomes than their younger counterparts.

Physicians and researchers who treat and study cancers, such as a type of incurable malignant brain tumor called glioblastoma multiforme (GBM), describe

this as "age-dependent outcome." Now researchers at Cedars-Sinai's Maxine Dunitz Neurosurgical Institute have directly linked this age factor to immune system cells recently produced by the thymus gland. Quantifying the number of these new thymus-derived lymphocytes actually provides a more accurate prediction of outcome than does patient age, and finding ways to boost these numbers may become a strategy for improving the ability of immunotherapy to fight cancer.

A more apt description than "age-dependent outcome" is "CD8+ recent-thymic emigrant-dependent outcome," according to an article in the Nov. 1 issue of the Journal of Immunology. CD8+ T lymphocytes that have recently entered the bloodstream from the thymus are called recent thymic emigrant (RTE) CD8+ T lymphocytes.

"Our findings suggest that levels and function of newly produced recent thymic emigrant CD8+ T cells critically influence age-dependent mortality and exert one of the strongest known influences on outcome," said Keith Black, director of the Dunitz Institute and Cedars-Sinai's Division of Neurosurgery and the Comprehensive Brain Tumor Program.

By quantifying the number of cells harboring CD8+ "T cell receptor excision circles" or TRECs, scientists can establish the number of CD8+ T lymphocytes that have recently emerged from the thymus. The researchers used TREC analysis to quantify CD4+ and CD8+ recent-thymic emigrant T cells in 44 patients with GBM. Twenty-four of these patients were newly diagnosed, while 18 had recurring disease. Seventeen of the patients were enrolled in immunotherapy vaccine trials.

Although thymic output of T cells declines as part of the normal aging process, and this decline parallels an increase in cancer progression, the specific impact of immunity on human tumor progression in general is not well understood. Because 11 of the vaccine trial patients were evaluated for immune activity against protein fragments common to a variety of human tumors, the researchers were able to examine the role of thymus output in age-dependent GBM outcome and anti-tumor immunity in general.

Patient statistics were analyzed by age and levels of RTE CD8+ T lymphocytes to determine the ability of each of these factors to predict GBM outcome independent of the other. High CD8+ levels predicted longer recurrence-free periods and overall survival in patients who were grouped by similar ages.

In contrast, lower patient age failed to predict outcomes in groups of patients who had similar RTE CD8+ levels. Based on this analysis, age predicts tumor outcome so well only because it loosely corresponds to CD8+ TREC levels. This implies that RTE CD8+ T cells are entirely responsible for older glioblastoma patients suffering such poor prognoses.

High levels of CD8+ TRECs also correlated with improved patient response to immune therapy.

Clinical Trials Approved By NCI

The National Cancer Institute's Cancer Therapy Evaluation Program Approved the following clinical research studies last month. For further information about a study, contact the principal investigator listed.

Phase II

Phase II Trial of BL22 Immunotoxin in Hairy Cell Leukemia. Lab of Molecular Biology, NCI, protocol 6048, Kreitman, Robert, phone 301-496-6947.

Phase II Trial of an Intradermally Administered MART-1/gp 100/Tyrosinase Peptide-Pulsed Dendritic Cell Vaccine Matured with a Cytokine Cocktail for Patients with Metastatic Melanoma. University of Southern California, protocol 6262, Weber, Jeffrey, phone 323-865-3360.

Phase II Study:Induction Cisplatin/Irinotecan Followed by Combination Carboplatin, Etoposide, 331, and Chest Radiotherapy in Limited Stage Small Cell Lung Cancer. Cancer and Leukemia Group B, protocol CALGB-30206, Kelley, Michael, phone 919-286-0411, ext.7.

Phase II Study of Cisplatin Plus Etoposide Plus Bevacizumab for Previously Untreated Extensive Stage Small Cell Lung Cancer. Eastern Cooperative Oncology Group, protocol E3501, Sandler, Alan, phone 615-343-4070.

Phase II Trial of CG8123, an Autologous Cancer Vaccine, in Patients with Selected Stage IIIB and IV Bronchioloalveolar Carcinoma. Southwest Oncology Group, protocol S0310, Davies, Angela, phone 916-734-3772.

Other

Pharmacokinetic Study of Methotrexate Using an Intratumoral Microdialysis Catheter. New Approaches to Brain Tumor Therapy Consortium, protocol NABTT-0302, Olson, Jeffrey, phone 404-778-5770.