Vol. 35 No. 2
February 2012

THE
CLINICAL CANCER LETTER

Cancer research news for clinicians

Lung Cancer

ASCO Recommends Beginning Palliative Care Alongside Standard Therapy in Metastatic NSCLC

The American Society of Clinical Oncology issued a provisional clinical opinion recommending that all patients with metastatic non-small cell lung cancer be offered palliative care along with standard cancer therapy, beginning at the time of diagnosis.

The opinion also states that palliative care should be considered early in patients with other metastatic cancers as well, although the available evidence is strongest for its use in metastatic lung cancer.

The guidance, published in the Journal of Clinical Oncology, was prompted by a growing body of research demonstrating the benefits of integrating palliative care into cancer therapy early, according to a statement from ASCO.

Palliative care can improve the quality of life for both patients and caregivers, but research showed that many patients were not referred to specialized care services until near the end of life, hampering efforts to address physical symptoms and meet the needs of patients.

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Colonoscopy

New Evidence Shows Polyp Removal Lowers Death Rate at 23-Year Follow-up

A new study showed that removing polyps by colonoscopy not only prevents colorectal cancer from developing, but also prevents deaths from the disease. Patients in the study were evaluated for up to 23 years after having the procedure.

"Our findings provide strong reassurance that there is a long-term benefit to removing these polyps and support continued recommendations of screening colonoscopy in people over age 50," said the study's lead author Ann Zauber, a biostatistician at Memorial Sloan-Kettering Cancer Center. The study was published in The New England Journal of Medicine.

Researchers evaluated the long-term results of 2,602 patients enrolled in the National Polyp Study who had precancerous polyps removed during colonoscopy.

They found that the detection and removal of these lesions resulted in a 53 percent reduction in colorectal cancer mortality.

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Concurrent Care Approach Causes No Harm, Adds Benefit

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"The Integration of Palliative Care into Standard Oncology Care" was developed by a panel of oncology and palliative experts convened by ASCO. The panel analyzed data from seven recently published randomized clinical trials involving patients with metastatic cancer that included a standard cancer care group and a "concurrent care" group, comprising patients receiving both standard cancer care and palliative care.

The panel's review found that the concurrent care approach caused no harm and was associated with a range of benefits, including comparable or improved survival, better symptom management, reduced depression, and improved caregiver and patient quality of life.

Concurrent care was also associated with lower overall resource use and cost. Palliative care leads to earlier and more frequent hospice referral, which in turn relieves symptoms, caregiver burden, and may improve survival, according to ASCO.

The authors noted that a primary concern is that reimbursement for early palliative care is not consistently available for patients who are undergoing active cancer therapy in an outpatient setting and are not enrolled in hospice care.

"Palliative care is about maintaining quality of life throughout the cancer journey," said Jamie Von Roenn, co-author of the opinion and professor of medicine in the Division of Hematology/Oncology at the Northwestern University Feinberg School of Medicine and Robert H. Lurie Comprehensive Cancer Center. "For patients with advanced cancer, the data are increasingly showing us that palliative care can be incredibly valuable for patients and their caregivers from the time they are diagnosed, not just at the end of life."

The opinion can be found here: http://bit.ly/wLWodX.

The Clinical Cancer Letter

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THE CLINICAL CANCER LETTER (ISSN 164-985X). Published monthly, subscription $129 per year, by The Cancer Letter Inc.

Kidney Cancer

AGS-003 Increased Survival In Combination with Sunitinib

Results from an open-label phase II study in patients with metastatic renal cell carcinoma demonstrated prolonged survival when treated with the immunotherapy AGS-003 in combination with sunitinib.

Based on the results, Argos Therapeutics Inc. plans to begin an international phase III trial, named ADAPT, comparing the addition of AGS-003 versus sunitinib alone in patients with newly diagnosed metastatic RCC.

Data from the phase II study were presented at the 2012 ASCO Genitourinary Cancers Symposium.

Multiple partial responses were observed, while 11 of 15 patients with serial immune assessments demonstrated increases in their CD28+ memory T cells. These immune responses correlated directly with prolonged survival in this study.

Overall, the median progression-free survival was 11.2 months and estimated Kaplan-Meier median overall survival was 29.3 months.

The study enrolled 21 patients with newly diagnosed, metastatic clear cell RCC. Following nephrectomy or metastasectomy to harvest tumor mRNA, autologous monocytes were collected by leukapheresis, in order to produce RNA-loaded dendritic cells specific to each patient's disease.

Treatment consisted of six-week cycles of sunitinib, four weeks on and two weeks off, with AGS-003 administered every three weeks for five doses, and then every 12 weeks until progression in combination with sunitinib.

Immune responses were evaluated at baseline and following five doses of AGS-003 using multiparametric flow cytometry, to assess the induction of anti-tumor, CD28+ memory T cell responses.

AGS-003 was well tolerated, with no immunotherapy-related serious adverse events observed.

Colonoscopy

At 23-Year Follow-up, Evidence Of Lower Cancer Death Rates

(Continued from page 1)

Furthermore, patients who had adenomatous polyps removed also had the same low death rate from colorectal cancer for up to 10 years after the procedure compared to a control group of people in which no such polyps were detected.

The multi-institutional study included experts from various disciplines, including endoscopists, radiologists, pathologists, epidemiologists and researchers from the following institutions: Boston University School of Medicine, Erasmus Medical Center, Minneapolis Veterans Administration, Valley Presbyterian Hospital, Cedars Sinai Medical Center, Medical College of Wisconsin, Mount Sinai Medical Center and Memorial Sloan-Kettering.

Colorectal Cancer

In Phase II Study, Vaccine IMA910 Stimulated Immune Response

Results from a phase II study in patients with advanced colorectal cell carcinoma showed that therapeutic cancer vaccine IMA910 was able to stimulate relevant immune responses against tumor-associated peptides. IMA910 comprises 13 tumor-associated peptides identified directly from colorectal cancer patients.

The study, presented at the 2012 ASCO Gastrointestinal Cancers Symposium, recruited 92 patients with advanced or metastatic colorectal cancer who had shown no progression following 12 weeks of first-line oxaliplatin-based chemotherapy and who had decided to take a 'drug holiday' from their chemotherapy regimen. The trial was conducted at 51 centers in nine European countries.

Patients received one single infusion of cyclophosphamide as an immunomodulator prior to the first vaccination with IMA910. Patients were treated with IMA910 plus granulocyte/macrophage colony stimulating factor, then split into groups treated with additional immunomodulator, imiquimod, or not.

All patients received up to 16 vaccinations with IMA910 over a period of nine months.

The study measured overall survival, disease control rate, T-cell responses to IMA910, the effect of imiquimod on immune response, the association of immune response with clinical benefit, and safety and tolerability.

The data from the study confirmed that IMA910 is able to stimulate relevant immune responses against the tumor-associated peptides in IMA910 in the majority of patients vaccinated.

When looking at the clinical outcome of patients who had detectable T cell responses against two or more of the tumor-derived peptides contained in IMA910, a consistently better clinical outcome was observed compared to those who did not have a detectable multi-T-cell response.

Moreover, patients who mounted both CD8+ and CD4+ multi-T-cell responses did not reach the median survival after more than 28 months of follow-up compared to a 16 months median survival time in patients those who did not mount those responses (HR 0.53; p=0.088).

IMA910 was well tolerated, with injection-site reactions being the most frequent side effect.

"The data that we have generated show a clear association between the patient's ability to mount an immune response to the tumor associated peptides in IMA910 and overall survival," said Carsten Reinhardt, chief medical officer of Immatics.

"Since the baseline characteristics of immune responders and non-responders were very similar in terms of risk factors, this strongly suggests a true clinical activity of this novel vaccine."

Ovarian Cancer

Researchers Identify Subtype Demonstrating Angiogenesis

Researchers have identified a subtype of ovarian cancer that is able to build its own blood vessels, suggesting that such tumors might be especially susceptible to anti-angiogenic drugs.

They estimate that the subtype may account for a third of all serous ovarian cancers. The discovery was made by analyzing data from the clinical records and tumor samples of more than 1,500 serous ovarian cancer patients. The study was published in PloS ONE.

"Unlike breast cancer, where we can distinguish different subtypes based on their genetic signatures, ovarian cancer has been viewed as a monolithically homogenous disease," said John Quackenbush, co-senior author and director of the Center for Cancer Computational Biology at the Dana-Farber Cancer Institute. "With this study, we've shown that serous ovarian cancer exists in at least one distinct subtype at

the molecular level, raising the possibility that it will be vulnerable to therapies directed at its molecular weaknesses."

Researchers scanned the activity of thousands of genes in high-grade serous ovarian cancers from 129 patients with an advanced stage of the disease. They then sifted the data using an algorithm called rISIS, which randomly assigns the tumor samples to different groups until it finds a grouping with a distinct set of genetic characteristics. That grouping represents a potential cancer subtype.

The algorithm yielded four possible subtypes of high-grade serous ovarian cancer, but only one of them held up when researchers applied a different technique for scanning gene activity. When researchers catalogued the genes that were highly expressed in that single subtype, many of the genes were known to be involved in angiogenesis.

Investigators analyzed data from ten published, independent studies of gene expression in serous ovarian cancer, involving 1,606 ovarian cancer patients. When investigators analyzed those medical records, they found that those with the angiogenic subtype tended to have more advanced, aggressive tumors.

The researchers believe that their classification of this new subtype has great potential to influence the treatment many patients receive and improve outcomes for a significant number of people with this disease. "The approach we've taken in this study offers a powerful way of identifying molecular subtypes of other cancers as well," said Quackenbush.

Prostate Cancer

MicroRNA Biomarkers Linked To Early-Stage Prostate Cancer

A clinical study linked microRNA biomarkers to clinical outcomes for patients with early-stage prostate cancer.

The study, presented at the 2012 ASCO Genitourinary Cancers Symposium, assessed the ability of specific microRNAs and genes to predict aggressive disease.

Investigators analyzed 416 prostate cancers from patients treated with radical prostatectomy at Cleveland Clinic between 1987 and 2004. Modified RT-PCR methodology was used to assess 76 microRNAs, a distinct class of biological regulators that are very small, averaging about 22 nucleotides in length.

Separately, Genomic Health Inc. initiated a clinical validation study and plans to announce topline results later this year.

The study was designed to determine if a multi-gene test can help patients with early stage prostate cancer by distinguishing aggressive disease requiring immediate treatment from indolent disease.

The study utilizes a RT-PCR process for analyzing very small amounts of formalin-fixed paraffin-embedded prostate tissue obtained by diagnostic prostate needle biopsy.

If positive, the clinical validation study results are expected to support the launch of the Oncotype DX prostate cancer test in 2013.

"In addition to supporting our development of a genomic prostate cancer assay to improve discrimination of clinically significant from insignificant prostate cancer, this study also demonstrates our innovative approach to provide a more comprehensive evaluation of biomarkers in the context of the known tumor heterogeneity of prostate cancer, one of the critical challenges faced by a biopsy-based clinical test for prostate cancer," said Steven Shak, chief medical officer of Genomic Health.

Researchers have also recently completed a study evaluating whether the expression of key genes and gene groups previously identified in radical prostatectomy specimens can be similarly predictive of aggressive prostate cancer when assessed in the small tissue volumes found in prostate needle biopsies.

The researchers plan to present the data at the 2012 American Association of Genitourinary Surgeons meeting in April.

Brain Tumors

Imaging Technique Identifies Consequences Of Mutation

Researchers have developed a new imaging technique that could eliminate the need for surgery in patients whose tumors are located in areas too dangerous to biopsy.

The magnetic resonance spectroscopy technique provides a diagnosis of cancer based on the imaging of a protein associated with a mutated gene found in 80 percent of low- and intermediate-grade gliomas.

In the study, published in Nature Medicine, researchers collected and analyzed biopsy samples from 30 glioma patients—half of which had the mutations and expected high levels of the protein. MRS imaging

of these patients was performed before surgery and predicted which patients had the mutation with 100 percent accuracy.

"To our knowledge, this is the only direct metabolic consequence of a genetic mutation in a cancer cell that can be identified through noninvasive imaging," said Elizabeth Maher, associate professor of internal medicine and neurology at UT Southwestern Medical Center and senior author of the study.

"This is a major breakthrough for brain tumor patients."

Researchers modified the settings of an MRI scanner to track the protein's levels. Previous research linked high levels of this protein to the mutation, and UT Southwestern researchers already had been working on MRS of gliomas to find tumor biomarkers.

"Our next step is to make this testing procedure widely available as part of routine MRIs for brain tumors. It doesn't require any injections or special equipment," said Maher.

Neuropathy

Researchers Call For New Approach To Peripheral Neuropathy Testing

Almost 25 percent of patients receiving neuropathy diagnoses undergo high-cost, low-yield MRIs, while very few receive low-cost, high-yield glucose tolerance tests, according to researchers are the University of Michigan.

Patients diagnosed with peripheral neuropathy are typically given many tests, but physicians are highly variable in their approach, according to the researchers. The study was published in the Archives of Internal Medicine.

Researchers used the 1996-2007 Health and Retirement Study to identify individuals with a diagnosis of peripheral neuropathy. They focused on 15 relevant tests and examined the number and patterns of tests six months before and after the initial diagnosis.

"Our findings, that MRIs were frequently ordered by physicians, but a lower-cost glucose tolerance test was rarely ordered, show that there is substantial opportunity to improve efficiency in the evaluation of peripheral neuropathy," said Brian Callaghan, assistant professor of neurology at the University of Michigan Medical School.

"Currently no standard approach to the evaluation of peripheral neuropathy exists," he said. "We need more research to determine an optimal approach."

"We know more and more people may develop peripheral neuropathy because it is commonly caused by diabetes," said co-author Kenneth Langa, professor of internal medicine at the university. "Our study suggests that the work-up currently used for neuropathy isn't standardized and tests that are less useful and more expensive may be used too often. We need a more efficient way to handle this increasingly common diagnosis."

Blood Analysis

Digital Microscope Blood Test Identifies Circulating Tumor Cells

Researchers demonstrated the effectiveness of an advanced blood test for detecting and analyzing circulating tumor cells. The findings showed that the blood analysis provides information that may be comparable to the information from surgical biopsies.

The findings were reported in five papers published in the journal Physical Biology.

"It's a next-generation technology," said Peter Kuhn, senior investigator of the new studies and associate professor at the Scripps Research Institute. "It significantly boosts our ability to monitor, predict, and understand cancer progression, including metastasis, which is the major cause of death for cancer patients."

The test, called HD-CTC, labels cells in a patient's blood sample to distinguish possible CTCs from ordinary red and white blood cells.

It then uses a digital microscope and an image-processing algorithm to isolate the suspect cells with sizes and shapes unlike those of healthy cells. Just as in a surgical biopsy, a pathologist can examine the images of the suspected CTCs to eliminate false positives and note their morphologies.

In the first study, researchers examined 83 advanced cancer patients using HD-CTC to document the test's sensitivity and accuracy for different cancer types.

The scientists found that the test detected five or more CTCs per milliliter of blood in 80 percent of patients with metastatic prostate cancer, in 70 percent of those with metastatic breast cancer, in 50 percent of those with metastatic pancreatic cancer, and in no healthy subjects.

Most patients whose CTC counts surpassed the detection threshold also showed small aggregates of CTCs, or microtumor emboli. In the second study, the test detected these aggregates in 43 percent of 71 patients

with advanced prostate, lung, pancreas, and breast cancers, and in none of a group of 15 healthy subjects.

In the third study, the team used the test to compare circulating tumor cells from prostate cancer patients with cells from prostate cancer cell lines that researchers often use as convenient models for prostate cancer biology in the lab.

The team found significant differences between the two classes of cells, in their cell morphology and in the way they were labeled by the tests fluorescent tags.

In the fourth study, the researchers performed the test on 28 patients with advanced non-small-cell lung cancer over periods of up to a year. The team was able to detect CTCs in 68 percent of samples, and found that the numbers of detected CTCs tended to go up as other measures showed cancer progression.

In the fifth and final study, researchers tested 78 patients who had just been diagnosed with various stages of non-small-cell lung cancer. "We demonstrated that we could sensitively detect CTCs even in patients with early-stage cancer," said Kuhn.

The studies involved researchers and oncologists at Scripps Health; UC San Diego Moores Cancer Center; the Billings Clinic; the University of California, San Francisco; the Center for Applied Molecular Medicine at the University of Southern California in Los Angeles; and the Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital.

Members of Scripps Research included: Dena Marrinucci, first author of the study "Fluid biopsy in patients with metastatic prostate, pancreatic and breast cancer"; Edward Cho, first author of "Characterization of circulating tumor cell aggregates identified in patients with epithelial tumors"; Daniel Lazar, first author of "Cytometric comparisons between circulating tumor cells from prostate cancer patients and the prostate-tumor-derived LNCaP cell Line"; Jorge Nieva, first author of "High-definition imaging of circulating tumor cells and associated cellular events in non-small cell lung cancer patients: a longitudinal analysis"; and Marco Wendel, with Lyudmila Bazhenova of UC San Diego Moores Cancer Center, as first authors of "Fluid biopsy for circulating tumor cell identification in patients with early and late stage non-small cell lung cancer; a glimpse into lung cancer biology."

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Lynch Syndrome

Study Links Breast, Pancreatic Cancer Risks to Lynch Syndrome

A prospective study provided the first strong evidence that patients with Lynch syndrome—an inherited disorder of cancer susceptibility caused by mutations in DNA repair genes—are at significantly higher risk for breast and pancreatic cancers.

The study also provided new, clearer estimates of the risks of cancers already associated with Lynch syndrome—including colon, uterus, ovary, kidney, stomach and bladder cancers. Researchers estimate that three to five of every 100 colon cancers are caused by Lynch syndrome.

While previous research has suggested higher risks of pancreatic cancer, the elevated risk of breast cancer was unexpected in this study.

Researchers followed a group of 446 carriers of one of four mismatch repair mutations related to Lynch Syndrome, as well as 1,029 of their relatives who did not carry these mutations. Participants were evaluated every five years at recruitment centers affiliated with the Colon Cancer Family Registry in Australia, New Zealand, Canada and the U.S.

After a median follow-up of five years, the researchers found that carriers had a 20-fold greater risk of colorectal cancer; a 30-fold greater risk of uterine cancer; a 19-fold higher risk of ovarian cancer; an 11-fold greater risk of kidney cancer; a 10-fold greater risk of pancreatic, stomach, and bladder cancers; and a four-fold greater risk of breast cancer. The study results were published in the Journal of Clinical Oncology.

The study also showed that relatives of patients with Lynch syndrome who do not carry related genetic mutations have no increased risk of developing cancer.

"Further clarification of the risk of breast cancer for women at various ages is needed to determine the recommended age for mammography for each patient, and to determine whether additional tests such as MRI are warranted for women with Lynch syndrome," said Mark Jenkins, senior author and associate professor at The University of Melbourne in Australia.

"Eventually, we expect that the management of cancer risk, including the choice and timing of screening, will be able to be tailored to the specific underlying gene mutation in a person with Lynch syndrome," said Jenkins. "Currently, individuals with the syndrome are typically advised to undergo colonoscopy at an earlier age and more frequently than the general population.

"However, there is no data demonstrating that

screening for these other cancers is beneficial, in part due to the absence of effective screening tests."

The researchers are continuing to follow this cohort. Since larger numbers of carriers are needed to determine cancer risks specific to each of the four genes for Lynch syndrome, they are establishing the International Mismatch Repair Consortium to pool data from 51 clinical research centers worldwide.

Collectively, these centers treat more than 7,500 families with Lynch syndrome and over 13,000 mismatch mutation carriers.

Genomics

Sarcoma, Li-Fraumeni Linked; Genetic Counseling Recommended

Researchers have drawn a link between sarcoma and Li-Fraumeni syndrome.

Genetic specialists at Dana-Farber/Children's Hospital Cancer Center are recommending that children being treated for sarcoma should be offered genetic counseling for this syndrome, a rare condition that greatly raises a person's risk of developing additional cancers.

The increased risk of cancer associated with the syndrome is caused by inherited changes in the tp53 gene. Fewer than 1,000 families with Li-Fraumeni syndrome have been identified worldwide, but research has shown that childhood sarcomas are one of the characteristic cancers associated with Li-Fraumeni syndrome.

Cancers typically diagnosed in patients with this syndrome include colon, stomach and breast cancers; sarcomas, including soft tissue and osteosarcomas, but not Ewing sarcoma; brain tumors, acute leukemia, and adrenal cortical carcinoma.

Fewer than 10 percent of children with sarcomas harbor a tp53 mutation, and while most children inherit the tp53 mutation from a parent, it's also possible for someone to be born with a new mutation.

Individuals who carry a tp53 mutation have a 50 percent chance of passing it on to each of his or her children.

Genetic counselors can provide families with the information they need to make informed decisions about whether or not to undergo genetic testing. People with Li-Fraumeni syndrome are especially sensitive to carcinogenic effects of radiation, which has been linked to the development of future cancers in some patients.

Knowing whether or not a child carries a tp53 mutation may influence how the doctors weigh the risks and benefits of radiation treatment.

In the coming months, Dana-Farber researchers will launch a new study to test the effectiveness of rapid full-body MRI scans for children and adults with Li-Fraumeni syndrome. The goal is to learn how to find cancers early and treat them effectively in people with Li-Fraumeni syndrome.

Breast Cancer

Pathology In Operating Suite Cuts Need for More Surgery

A new service cut the number of additional breast cancer surgeries by 64 percent, down to one of every 10 women. Normally, nearly one in three women who have breast cancer surgery will need to return to the operating room after the tumor has been evaluated by a pathologist.

The University of Michigan Comprehensive Cancer Center puts pathologists in the operating suite to assess tumors and lymph nodes immediately after they are removed. The surgeon and patient remain in the operating room until results confirm whether or not additional tissue or lymph nodes need to be removed.

A study evaluating 271 patients treated eight months before and 278 patients treated eight months after the beginning of this program was published in the American Journal of Surgery.

Before the on-site pathology, 25 percent of patients needed a second operation to remove more tissue, compared to 11 percent after the service began. Among patients with cancerous lymph nodes, 93 percent of them avoided a second surgery with on-site pathology.

In addition, the study found that assessing the margins in the OR allowed more women to conserve their breasts.

"The frequent need for second surgeries among patients undergoing breast cancer surgery represents a tremendous burden for patients," said lead author Michael Sabel, associate professor of surgery at the university. "Our experience shows that offering on-site pathology consultation has a substantial impact on quality of care."

Establishing on-site pathology requires a different technique for preserving and evaluating the cells, called frozen section analysis. After this is completed, pathologists then process the tumors for standard testing using traditional methods. The study showed consistent results across both types of analysis.

On-site pathology using frozen tissue sections is offered at a handful of academic medical centers across

the country. Obstacles include transporting the tissue samples, building a pathology facility, and staffing it appropriately at an offsite surgical center.

"In large part, routine intraoperative analysis of lumpectomy margins is rare because of logistical issues, especially as breast surgery is more commonly performed at outpatient surgical centers," said Sabel.

"Despite these obstacles, we found that not only is this beneficial for our patients, but it reduced the costs of caring for patients with breast cancer."

Biostatistics

UHC Expands Risk Models To Include 25 Cancer Variables

UHC expanded and refined the risk-adjusted models in its Clinical Data Base/Resource Manager to include 20 pediatric-specific risk models. Data from pediatric patient discharges are now modeled separately from the adult discharges.

The changes also include enhanced variables for models in which the primary diagnosis is not cancer, but the majority of patients have a secondary oncology diagnosis.

With the new models, users can stratify studies by different age groups and benchmark against peers on the variables most relevant to pediatric populations, giving a potentially more accurate picture of which hospital treatments are most effective for children.

Previously, the risk models reflected the overall effect of solid tumor cancers. Now members can see the specific impact of cancers on mortality, length of stay, and costs. The three general cancer variables have been expanded to more than 25 specific variable candidates.

Both the pediatric and the oncology risk models were developed with input from UHC's Risk Adjustment Task Force. Member input from MD Anderson Cancer Center and City of Hope also contributed to the oncology model.

The risk model changes will be applied to all cases starting with patients discharged from the fourth quarter of 2008 going forward. UHC will continue to support the old risk models through the third quarter of 2012 to give members enough time to finish their population trending studies.

UHC will no longer provide expected values for the old models after third quarter 2012 discharges are loaded.

Trials Approved by NCI CTEP For The Month of February

The National Cancer Institute Cancer Therapy Evaluation Program approved the following clinical research studies last month. For further information, contact the principal investigator listed.

Phase I

9101: Administration of Tumor-Associated Antigen (TAA)-Specific Cytotoxic T-Lymphocytes to Patients with Active or Relapsed Hodgkin or Non-Hodgkin Lymphoma. Baylor College of Medicine; Bollard, Catherine Mary. (832) 824-4781

Phase II

8867: Randomized Phase II Trial of MAP Kinase Inhibition with AZD6244 Hydrogen Sulfate in Combination with MK-2206 (Akt Inhibitor) in Patients with BRAF V600E Mutant Advanced Melanoma Who Have Previously Failed Prior Therapy with a Selective BRAF inhibitor (PLX4032/RG7204 or GSK2118436). Moffitt Cancer Center and Research Institute; Sosman, Jeffrey A. (615) 936-3831

RTOG-1106: Randomized Phase II Trial of Individualized Adaptive Radiotherapy Using During-Treatment FDG-PET/CT and Modern Technology in Locally Advanced Non-Small Cell Lung Cancer (NSCLC). Radiation Therapy Oncology Group. Kong, Feng-Ming Phoenix; (734) 936-7810.

S1117: A Randomized Phase II Study of Azacitidine in Combination with Lenalidomide vs. Azacitidine Alone vs. Azacititdine in Combination with Vorinostat for Higher-Risk Myelodysplastic Syndromes (MDS) and Chronic Myelomonocytic Leukemia (CMML). Southwest Oncology Group; Sekeres, Mikkael Aaron. (216) 445-9353.

Other Phases

AALL12B2: Signaling in Tumorigenesis and Immunity. Children's Oncology Group; Xiao, Gutian. (412) 623-5410

AAML12B3: Analysis of MicroRNA Expression in Down Syndrome Acute Myeloid Leukemia and the Transient Myeloproliferative Disorder. Children's Oncology Group; Taub, Jeffrey Warren; (313) 745-5515.

ANBL12B2: Genome Based Outcome Prediction in High Risk Neuroblastoma. Children's Oncology Group; Cohn, Susan Lerner. (773) 702-2571.

ANBL12B5: Alternative Lengthening of Telomeres (ALT) in Neuroblastoma. Children's Oncology Group; Lau, Loretta. 9845-3115.

S1105: Randomized Trial of Text-Messaging Intervention to Reduce Early Discontinuation of Adjuvant Aromatase Inhibitor Therapy in Women with Early Stage Breast Cancer. Southwest Oncology Group; Neugut, Alfred I. (212) 305-9414.

Pilot Phase

8992: A Pilot Study of Sorafenib in Patients with Acute Myeloid Leukemia as Peri-Transplant Remission Maintenance. Johns Hopkins University; Pratz, Keith William. (410) 502-7726

FDA News

Agency Expands Gleevec Label To Include Rare GIST Subset

FDA approved Gleevec for expanded use in patients with a rare subset of gastrointestinal stromal tumor.

FDA granted Gleevec (imatinib) regular approval for use in adult patients following surgical removal of CD117-positive gastrointestinal stromal tumors.

Clinical data from a large, randomized clinical study comparing 12 to 36 months of Gleevec showed that 36 months of the drug significantly prolonged overall survival and progression-free survival.

At 60 months, 92 percent of patients who received 36 months of Gleevec were alive, compared to 82 percent of patients who received 12 months of Gleevec.

"The development of Gleevec over the past decade highlights the need to further study drugs after approval to truly characterize their benefits," said Richard Pazdur, director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "Although originally approved in the metastatic disease setting, this subsequent trial has demonstrated that longer use of Gleevec can prolong patient's lives in earlier disease settings."

Gleevec was originally granted accelerated approval in 2002 for the treatment of advanced or metastatic GIST. In 2008, Gleevec received accelerated approval for the adjuvant treatment of patients with GIST who had potentially curative resection of tumors, but were at increased risk of recurrence. Regular approval for the metastatic GIST indication was also granted in 2008.

Gleevec was first approved in 2001 to treat patients with advanced, Philadelphia chromosome-positive, chronic myeloid leukemia. Gleevec is marketed by Novartis Pharmaceuticals Corp.

* * *

FDA and industry representatives reached an agreement in principle on recommendations for the third reauthorization of a medical device user fee program.

The proposed recommendations would authorize FDA to collect $595 million in user fees over five years, plus adjustments for inflation. The details of the agreement are expected to be finalized soon, according to a statement from FDA. The current Medical Device User Fee Act of 2007 is set to expire Sept. 30.

The agreement comes after a year of negotiations between the agency and the industry. With the additional funding, FDA plans to hire over 200 full-time equivalent works by the end of the program, and the agency expects that the agreement will result in a reduction in average total review times.

FDA says the agreement would result in greater accountability, predictability and transparency, and would include improvements such as a more structured pre-submission process and earlier interactions between the agency and applicants.

The industry associations who have reached an agreement in principle with the FDA include the Advanced Medical Technology Association, the Medical Device Manufacturers Association and the Medical Imaging and Technology Alliance.

Once the final details of the agreement are completed, FDA will present a package of proposed recommendations for public comment, before submitting them to Congress for approval. The date of the public meeting has yet to be determined.