Vol. 34 No. 10
October 2011

THE
CLINICAL CANCER LETTER

Cancer research news for clinicians

Breast Cancer

Herceptin Regimen Minus Adriamycin Increases Survival With Less Toxicity

Treating women with early-stage breast cancer with a combination of chemotherapy and Herceptin significantly increases survival in patients with HER-2 positive disease, according to a study published in the New England Journal of Medicine.

The study data also showed that Adriamycin (doxorubicin) was not a necessary part of an early-stage breast cancer treatment regimen. Adriamycin can cause permanent heart damage, especially when paired with Herceptin (trasuzumab).

"We're encouraged that the survival advantages found in this study have been maintained and continue to be significant," said lead author Dennis Slamon, director of clinical/translational research at UCLA's Jonsson Comprehensive Cancer Center, whose laboratory and clinical research led to the development of Herceptin. "I believe there's room for even further improvement."

(Continued to page 2)

NSCLC

Alimta Reduces Risk Of Progression In Patients Aged 70 Years or Older

Results from a subgroup analysis of data from the phase III PARAMOUNT study showed that continuation maintenance therapy with Alimta (pemetrexed for injection) also reduces the risk of disease progression in patients aged 70 years or older with advanced, nonsquamous, non-small cell lung cancer.

A total of 939 patients with advanced nonsquamous NSCLC were enrolled in the study; 539 did not progress during the induction phase and entered the maintenance phase of the trial. Of those, 92 patients were elderly.

The analysis compared Alimta to placebo in elderly patients aged 70 years or older. In the group of elderly patients, Alimta reduced the risk of disease progression by 65 percent (HR=0.35; 95% CI: 0.20-0.63), based on a median progression-free survival of 6.4 months on the Alimta arm compared with 3.0 months on the placebo arm.

In the group of patients younger than 70 years of age, Alimta reduced the risk of progression by 31 percent (HR=0.69, 95% CI: 0.54-0.90), with

(Continued to page 3)

PO Box 9905
Washington DC 20016
Telephone 202-362-1809

Adriamycin Not Necessary In Early-Stage Regimens

(Continued from page 1)

The three-armed study compared the standard therapy of Adriamycin and Carboplatin followed by Taxotere (ACT), the same regimen plus one year of Herceptin (ACTH), and a regimen of Taxotere and Carboplatin with one year of Herceptin (TCH).

The study showed survival advantage for patients in the Herceptin-containing arms, with 92 percent of patients on ACTH and 91 percent of patients on TCH still alive at five years, compared to 87 percent in the ACT arm. Estimated disease-free survival, or the time from treatment to recurrence, was 75 percent the ACT arm, 84 percent among those receiving ACTH and 81 percent in the TCH arm.

The women who received Adriamycin and Herceptin had a five-fold greater increase of experiencing congestive heart failure and a two-fold increase of sustained cardiac dysfunction without symptoms. The women also experienced worse acute toxicities, such as nausea, diarrhea, vomiting, neuropathy, fatigue and falling white blood counts.

"Given the data in this study, it makes one really question what role Adriamycin should play in the treatment of HER-2 positive early breast cancer, or in the treatment of early breast cancer at all," Slamon said.

"This trial should impact the way these breast cancers are treated, with a non-anthracycline regimen being our preferred option. I think this is a change that is going to be slow in coming, unfortunately, as many of our adjuvant treatments for breast cancer are built on the backbone of anthracyclines. While they're effective, whatever gain patients may receive is more than made up for in the serious and chronic long-term side effects."

The study was conducted by the Breast Cancer International Research Group, and enrolled 3,222 women with early stage breast cancer between April 2001 and March 2004. Patients were randomized to one of the three arms. The study's primary endpoint was disease-free survival, but it also measured overall survival, safety, including cardiac toxicities, pathologic and molecular markers and quality of life.

The Clinical Cancer Letter

Editor and Publisher: Paul Goldberg
Copy Editor: Conor Hale
Intern: Lucas Thomas

Editorial, Subscriptions, and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
Website: http://www.cancerletter.com

THE CLINICAL CANCER LETTER (ISSN 164-985X). Published monthly, subscription $125 per year, by The Cancer Letter Inc.

Breast Cancer

Family History of BRCA Mutation Does Not Equal Increased Risk

Close relatives of women who carry mutations in a BRCA gene—but who themselves do not have such genetic mutations—do not have an increased risk of developing breast cancer, according to a study published in the Journal of Clinical Oncology.

This population-based analysis counters a 2007 study that indicated first-degree relatives of women with BRCA gene mutations are several times more likely to develop breast cancer. These new findings suggest that women who do not have the mutation may not need extra cancer screening or other increased preventive measures.

Women who inherit a mutation in the BRCA1 or BRCA2 gene carry a five- to 20-fold higher risk of developing breast or ovarian cancers. First-degree relatives who have not inherited the same familial BRCA mutation have been considered to have a considerably lower risk for breast cancer.

Investigators studied women with breast cancer in 3,047 families in three population-based cancer registries in Northern California (1,214), Australia (799) and Canada (1,034). They found 292 families in which a woman had a BRCA mutation.

They compared the risk of breast cancer among first-degree relatives of breast cancer patients who did and did not carry a BRCA mutation and found no significant difference.

"This new study gives reassurance to non-carriers that they do not have an increased risk due to the familial mutation, and should be regarded the same as other non-carriers with first-degree relatives who have had breast cancer," said study first author Allison Kurian, assistant professor of medicine and health research and policy at Stanford University School of Medicine.

The 2007 study showed that women who tested

negative for a specific familial BRCA mutation had a two- to five-fold increased risk of developing breast cancer. Kurian said that the study had looked at women who were in cancer family clinics and compared their breast cancer risk to that of women in the general population.

Women from cancer family clinics were more likely to have intensive screening, and breast cancer risks tend to be higher among close relatives of breast cancer patients than those in the general population.

"The control group we used—relatives of breast cancer patients in families without a BRCA mutation—was important," said senior author Alice Whittemore, professor of epidemiology and biostatistics at Stanford.

"The results suggest that women who test negative for their family's BRCA mutation have no greater breast cancer risk than a woman who also has relatives with breast cancer but no family-specific mutation."

Prostate Cancer

Daily Vitamin E Supplements Can Lead to Increased PCa Risk

Men who took 400 international units of vitamin E daily had more prostate cancers compared to men who took a placebo, according to an updated review of data from the Selenium and Vitamin E Cancer Prevention Trial (SELECT).

The study, published in the Journal of the American Medical Association, showed that there were 76 prostate cancers per 1,000 men who took only vitamin E supplements, versus 65 in men on placebo over a seven-year period. This represents a 17 percent increase.

SWOG carried out SELECT at more than 400 clinical sites in the U.S., Puerto Rico, and Canada. SELECT was funded by NCI and NIH.

"Based on these results and the results of large cardiovascular studies using vitamin E, there is no reason for men in the general population to take the dose of vitamin E used in SELECT as the supplements have shown no benefit and some very real risks," said Eric Klein, a SELECT study co-chair, and a physician at the Cleveland Clinic.

"For now, men who were part of SELECT should continue to see their primary care physician or urologist and bring these results to their attention for further consideration."

The SELECT study began in 2001 and included over 35,000 men. Because of this latest finding, researchers are encouraging all participants to consider taking part in long-term study follow-up so investigators can continue to track outcomes.

Digital Immunoassay PSA Test May Predict Cancer Recurrence

A pilot study found that digital immunoassay for prostate-specific antigen can be a reliable predictor of five-year recurrence free survival following radical prostatectomy.

The study, published online by the British Journal of Urology International, examined Quanterix Corporation's Single Molecule Array technology.

Researchers utilized frozen serum specimens from men who had undergone radical prostatectomy and had no evidence of biochemical recurrence. The single molecule PSA assay was used to measure PSA levels in all men following surgery.

Researchers found that PSA nadir value was a significant predictor of biochemical recurrence.

All of the men with low PSA nadir values did not develop recurrence, but 63 percent of men with higher PSA values eventually recurred. The sensitivity and specificity values of the test were 100 and 75 percent, respectively. The positive and negative predictive values were 69 and 100 percent, respectively.

"These results have important implications for the way prostatectomy patients will be managed in the future," said Herbert Lepor, chairman of the Department of Urology at NYU School of Medicine.

"Not only will physicians be able to reassure patients who are at low risk of recurrence following radical prostatectomy, but the identification of a reliable predictor of recurrence soon after surgery has important implications for the frequency of PSA testing and selection of candidates for adjuvant therapy. In addition to providing patients with peace of mind, implementation of this test could lead to a reduction in healthcare costs."

NSCLC

Alimta Reduced Progression Risk By 61 Percent In Senior Patients

(Continued from page 1)

a progression-free survival of 4.0 months compared to 2.8 months for placebo.

"Lung cancer can be challenging to treat in patients over 70 years of age because they often have comorbidities and may be less tolerant of anti-cancer therapies," said Cesare Gridelli, a clinical trial investigator for the PARAMOUNT study and physician with S. Giuseppe Moscati Hospital in Avellino, Italy.

"In fact, some patients over the age of 70 may simply be offered supportive care alone. These results show that an ALIMTA maintenance regimen could provide benefit to certain elderly patients."

The study included patients who received Alimta in combination with cisplatin induction therapy. Patients whose disease had not progressed during the Alimta plus cisplatin induction and had a performance status of 0-1 were randomized to receive Alimta maintenance plus best supportive care or placebo plus best supportive care until disease progression.

Overall, the most serious drug-related adverse events were higher for elderly patients treated with Alimta continuation maintenance, compared with patients less than 70 years of age (21 percent vs. 7 percent, respectively).

These adverse events were primarily hematological, including anemia and neutropenia. Elderly patients in the study tended to have a poorer performance status than younger patients (PS 0: 20 percent vs. 34 percent, respectively; PS 1: 79 percent vs. 66 percent, respectively), and the older group received more cycles of Alimta therapy (5.5 vs. 4.8 in the younger group).

Overall results of PARAMOUNT, which met its primary endpoint of progression-free survival, were presented in June 2011 at the American Society of Clinical Oncology Annual Meeting.

Talactoferrin Second-Line Therapy Increases Survival In Stage IIIB/IV

A phase II study showed that talactoferrin, an oral immunotherapy for patients with previously treated non-small cell lung cancer, achieved its primary endpoint of improvement in overall survival.

The randomized, placebo-controlled study was published in the Journal of Clinical Oncology, showing that talactoferrin appeared to improve survival across a range of patient subsets, including patients with squamous and non-squamous disease and other prognostic factors.

The study enrolled 100 patients with stage IIIB/IV non-small cell lung cancer whose disease had progressed following one or more lines of anti-cancer therapy.

The results showed that talactoferrin plus best supportive care improved median overall survival by 65 percent compared to placebo plus best supportive care [6.1 months versus 3.7 months, HR=0.68, 90% CI: 0.47-0.98, p=0.04 (one-tailed log-rank test)], meeting the protocol-defined level of statistical significance.

The six-month overall survival rate was 30 percent in the placebo arm and 52 percent in the talactoferrin arm. The one-year overall survival rate was 16 percent in the placebo arm compared to 29 percent in the talactoferrin arm. Supportive results were seen in the secondary endpoints of progression-free survival and disease control rate.

"Talactoferrin appears to provide anti-tumor activity without many of the common toxicities associated with other treatments for non-small cell lung cancer," said Rajesh Malik, chief medical officer of Agennix AG.

Talactoferrin was shown to be very well tolerated in this study, with fewer adverse events compared to placebo. The most frequently reported grade 3 or greater adverse event was dyspnea, occurring in 15 percent of patients in the talactoferrin arm and 26 percent in the control arm. There were no serious adverse events considered to be related to treatment.

Two phase III trials with talactoferrin in NSCLC are ongoing. The FORTIS-M trial, which completed enrollment in March 2011, is evaluating talactoferrin in NSCLC patients whose disease has progressed following two or more prior treatment regimens.

A second phase III trial—FORTIS-C—is evaluating talactoferrin in combination with the standard chemotherapy regimen, carboplatin/paclitaxel, in first-line NSCLC patients.

Agennix is also developing talactoferrin for the treatment of severe sepsis and has initiated a phase II/III trial, called OASIS, in that indication.

Colorectal Cancer

Researchers Discover Bacteria Common in Colon Cancer Tissue

For the first time, a specific microorganism has been found to be associated with human colorectal cancer.

In two studies published online in Genome Research, two independent research teams have found a single genus of bacteria, Fusobacterium, more often in colon cancer tissue than in normal tissues.

Gastric cancers have been previously linked to inflammation mediated by the microorganism H. pylori, so it is possible that some of the many species of microbes found in the gut could be associated with colorectal cancers.

"This was especially surprising because although

Fusobacterium, the bacterium we found in colon tumors, is a known pathogen—it is a very rare constituent of the normal gut microbiome and has not been associated previously with cancer." said Robert Holt of the BC Cancer Agency and Simon Fraser University, and senior author of one of the reports.

"It was also surprising that Fusobacterium has also previously been reported to be associated to be with ulcerative colitis, which is itself a risk factor for colon cancer," noted Matthew Meyerson of the Dana-Farber Cancer Institute and senior author of the other study.

Holt's group identified Fusobacterium by sequencing the RNA present in colon cancer tissue and compared this to RNA from normal colon tissue, looking for sequences that originate from microorganisms, while Meyerson's team sequenced the DNA present in the cancer tissues and normal tissues to find microbial sequences.

Holt and Meyerson both noted that although it is unclear at this time whether Fusobacterium infection is a cause or consequence of colorectal tumors, the microbe could prove to be very useful in the clinic as a marker for cancer. If Fusobacterium is found to be causative for disease, clinical trials could evaluate the effectiveness of antibiotics or vaccines to treat or prevent cancer.

Colon Cancer Survival Rates Differ Across Racial Lines

African-American patients with resected stage II and stage III colon cancer experienced worse overall and recurrence-free survival compared to whites, but similar recurrence-free intervals, according to a study published in JNCI.

The 5-year relative survival rates for black and white colorectal cancer patients between 1999 and 2005 were 57 and 68 percent.

Of the estimated 146,970 new colorectal cancer cases in 2006, 15,000 were projected to occur in individuals of African ancestry, resulting in approximately 7,000 deaths.

Although several causes of the disparities have been identified, the reasons are not well understood.

In order to determine the disparities of colorectal cancer survival outcomes between blacks and whites, Greg Yothers, of the National Surgical Adjuvant Breast and Bowel Project Biostatistical Center, and his colleagues examined data from the Adjuvant Colon Cancer ENdpoinTs (ACCENT) collaborative group database to analyze 14,611 African-American and white patients with stage II or III colorectal cancer enrolled in 12 phase III randomized controlled clinical trials conducted in North America from 1977-2002.

Within these trials, patients received the same adjuvant colon cancer therapy regardless of race, but care for other diseases or recurrent colon cancer was outside the scope of these trials.

The researchers evaluated overall survival, recurrence-free survival, and recurrence-free interval.

The researchers found that the five-year overall survival rate was worse among the 1,218 African-American patients, compared to the whites, with a 4.6 percentage point decrement in 5-year survival, and a 3.7 percentage point decrement in recurrence-free survival. There was no statistically significant difference in recurrence-free interval.

The authors wrote that the survival differences are most likely because of factors unrelated to a patient's response to adjuvant treatment.

"Black patients with resected stage II and III colon cancer treated with identical adjuvant therapy experienced poorer overall and recurrence-free survival but similar recurrence-free interval compared with white patients," they wrote. "Biological differences, differences in general health, and disparities in health care outside the clinical trial are possible explanations for these findings."

In an accompanying editorial, Olufunmilayo Olopade, director of the Center for Clinical Cancer Genetics and Global Health at the University of Chicago, and his colleagues wrote that the Yothers study is consistent with studies published in the last decade.

"When treated equally, African-Americans have similar colon cancer-specific survival but continue to have poorer overall survival compared with white patients," they wrote.

Going forward, trials must include basic information on patients' socio-demographic situation, as well as their tumor biology and co-morbid conditions, the editorialists wrote, adding that primary care of survivors should also be improved and monitored so that differences in survival after recurrence can be better understood.

Lastly, trials examining genetic markers may require enrollment targets, so that a trial could close to accrual for whites but may remain open for African-Americans and other minorities.

The editorialists wrote, "We have documented racial and ethnic differences in cancer survival by looking from 10,000 feet over the past decade, but it is past time for us to get out of the clouds and collect and integrate data that advance the field."

Survivorship

NCI Predicts 42 Percent Increase In Number of Senior Survivors

NCI researchers are predicting a 42 percent increase in the number of cancer survivors 65 years of age and older over the next decade.

The study, published in Cancer Epidemiology, Biomarkers and Prevention, said the number of survivors will increase from 8 million to over 11 million, including newly diagnosed patients and long-term survivors.

Researchers concluded this pattern is mainly the result of the aging U.S. population.

Julia Rowland, director of NCI's Office of Cancer Survivorship, and her colleagues analyzed data from the NCI SEER program. They found that, following the signing of the National Cancer Act of 1971, the entire U.S. cancer survivor population, including all age groups, totaled approximately three million, increasing to nearly 12 million in 2008.

Exceptions to this pattern are breast cancer and ovarian cancer, in which the majority of cases occur in younger populations.

The most common diagnoses among cancer survivors include: female breast cancer, 22 percent; prostate cancer, 20 percent; and colorectal cancer, at 9 percent.

The researchers warn that treating this growing age group will present special concerns and challenges to health care providers.

Radiation Therapy

IMRT Less Toxic Than 3D-CRT In Localized Prostate Cancer

A preliminary analysis of a phase III dose-escalation study found that treatment with IMRT is associated with fewer gastrointestinal and genitourinary toxicities than treatment using 3D-CRT.

The study compares high-dose three-dimensional conformal radiotherapy to intensity-modulated radiation therapy, measuring improvements in overall survival in patients with localized prostate cancer.

The trial was developed to determine whether the higher doses of radiation therapy shown achievable with 3D-CRT in single-institution studies and an early-phase RTOG trial are justified by an improvement in local tumor control, freedom from prostate-specific antigen failure, and overall survival. Due to its growing availability, IMRT was included as a treatment option after the first year.

The analysis was presented at a plenary session at the American Society for Radiation Oncology's annual meeting in Miami.

Of the 748 evaluable study participants randomized to the high-dose (79.2 Gy) treatment arm, 491 received 3D-CRT and 257 received IMRT, each for a total of 44 treatments, with a median follow-up of 4.6 years and 3.5 years, respectively.

Patients who received IMRT showed statistically significant reduction in GU and GI adverse events occurring within 90 days following treatment.

The study also demonstrated a trend for a clinically meaningful reduction in later GI side effects. In addition, researchers noted that acute GI side effects and high radiation doses to large volumes of the rectum were significantly associated with late rectal side effects.

A quality of life analysis evaluating patients after 3D-CRT and IMRT high-dose treatment compared patient-reported erectile, bowel and bladder function outcomes through questionnaires.

To assess erectile dysfunction outcomes, a baseline International Index of Erectile Function (IIEF) questionnaire was completed by 507 study participants.

At six, 12, and 24 months post-treatment, 56 percent, 65 percent, and 61 percent of the participants, respectively, completed the IIEF.

The Functional Alterations due to Changes in Elimination (FACE) questionnaire was completed at baseline by 499 participants in the high-dose arm to assess outcomes related to bowel and bladder function.

At three, six, 12, and 24 months post-treatment, 48 percent, 63 percent, 74 percent, and 66 percent of study participants, respectively, completed the FACE.

While no significant differences were shown between the two treatment methods, researchers point out that this patient-reported data should not be interpreted alone, but must be taken into consideration in any comparative effectiveness analysis.

NCI CTEP: Approved Trials For The Month of October

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

Pilot Phase

8836: Pilot and Translational Study of Dasatinib (NSC#732517) Paclitaxel and Carboplatin in Women with Advanced Stage and Recurrent Endometrial Cancer. MD Anderson Cancer Center, Coleman, Robert L. (713) 745-3357

Phase 0

GOG-8030: A Comparative Effectiveness Study of Cancer Risk Management for Women at Elevated Genetic Risk of Ovarian Cancer. Gynecologic Oncology Group, Havrilesky, Laura J. (919) 684-3765

Phase I

8484: Phase 1 Trial of ABT-888 and SCH727965 without or with Carboplatin in Patients with Advanced Solid Tumors. Dana-Farber Cancer Institute, Shapiro, Geoffrey Ira. (617)632-4942

9119: Phase I Study of AR-42 in Relapsed Myeloma, Chronic Lymphocytic Leukemia, and Lymphoma. Ohio State University Medical Center, Hofmeister, Craig. (614) 293-3507

Phase I/II

8871: Phase I/II Study of Entinostat and Lapatinib in Patients with HER2-Positive Metastatic Breast Cancer in Whom Trastuzumab Has Failed. MD Anderson Cancer Center, Ueno, Naoto Tada. (713) 792-2817

Phase II

8854: Randomized Phase II Study of Epigenetic Priming Using Decitabine with Induction Chemotherapy in Patients with Acute Myelogenous Leukemia (AML). Montefiore Medical Center, Scandura, Joseph Michael. (212) 746-2072

8984: A Phase II Study of c-Met Inhibitor ARQ 197 in Patients with Relapsed Multiple Myeloma. MD Anderson Cancer Center, Orlowski, Robert Zygmunt. (713) 745-8576

ACNS1021: A Phase II Study of Sunitinib (NSC# 736511, IND# 74019) in Recurrent, Refractory or Progressive High Grade Glioma and Ependymoma Tumors in Pediatric and Young Adult Patients. Children's Oncology Group, Wetmore, Cynthia J. (901) 595-6275

Phase II/III

NCCTG-N10C2: A Double-Blind, Placebo-Controlled Study of Magnesium Supplements to Reduce Menopausal Hot Flashes. North Central Cancer Treatment Group, Loprinzi, Charles Lawrence. (507)284-1623

Other Phase

AAML11B12: Validation of a Classifier for the Prediction of Risk of Relapse Using Single Cell Network Profiling (SCNP) Assays for Childhood AML. Children's Oncology Group, Lacayo, Norman James. (650) 723-5535

ABTR12B1: Gene Expression (GE) and MicroRNA (MIRNA) Expression Profiles of Malignant Rhabdoid Tumors (MRT) of the Kidney (RTK) and Atypical Teratoid Rhabdoid Tumor (ATRT). Children's Oncology Group, Sredni, Simone Treiger. (773) 755-6526

AEPI10N1: Molecular Epidemiology of Pediatric Germ Cell Tumors. Children's Oncology Group, Poynter, Jenny N. (612) 625-4232

AGCT11B2: Genomic Signatures of Malignant Germ Cell Tumor Progression: A Retrospective Study of Banked Specimens. Children's Oncology Group, Amatruda, James Francis. (214) 648-3896

ARST11B5: Comprehensive Genome Sequencing of Desmoplastic Small Round Cell Tumors. Children's Oncology Group, Hingorani, Pooja. (602) 546-0920

ARST12B1: A Retrospective Study on the Diagnostic Value of Serum miR-206 in Rhabdomyosarcoma. Children's Oncology Group, Hosoi, Hajime. 75-251-5571

ECOG-E5103A-ECOG-ICSC: Biomarker Prediction of Chemotherapy-Related Amenorrhea in Premenopausal Women with Breast Cancer Participating in E5103. Eastern Cooperative Oncology Group, Ruddy, Kathryn J. (617) 632-4587

S8600-S9031-S9333-A: Identification of Differentially Methylated Genomic Regions That Are Prognostically Significant in AML. Southwest Oncology Group, Fang, Min. (206) 288-1385

FDA News

FDA Grants Accelerated Approval To Ferriprox for Iron Overload

FDA gave accelerated approval to Ferriprox (deferiprone) for iron overload due to blood transfusions in patients with thalassemia, a genetic blood disorder that causes anemia, who had an inadequate response to prior chelation therapy.

The approval sets a precedent, as the agency for the first time approved an application based on a retrospective review of data.

The FDA Oncologic Drugs Advisory Committee accepted this lower level of evidence, voting 10-2 to recommend approval, departing from its usual insistence of prospective clinical trials.

The advisory committee—and the agency—also accepted extensive international experience with the drug as evidence supporting its safety and efficacy (The Cancer Letter, Sept. 30).

Patients with thalassemia have excess iron in the body from the frequent blood transfusions (transfusional iron overload), a condition that is serious and can be fatal. These patients also have a risk of developing liver disease, diabetes, arthritis, heart failure or an abnormal heart rhythm.

The standard of care to treat transfusional iron overload is chelation therapy—chemical agents that are used to remove heavy metals from the body. Ferriprox is intended for use when chelation therapy is inadequate.

Ferriprox is marketed by ApoPharma Inc. of Toronto.

ApoPharma has agreed to several post-marketing requirement and commitments. One commitment includes further study of the use of Ferriprox in patients with sickle cell disease who have transfusional iron overload.

"Ferriprox represents the first new FDA-approved treatment for this disorder since 2005," said Richard Pazdur, director of the Office of Hematology and Oncology Products in the FDA Center for Drug Evaluation and Research

Earlier this year, HHS launched the Sickle Cell Disease Initiative bringing together HHS agencies to enhance the quality and quantity of SCD data, develop best practice guidelines and quality of care metrics, improve health care delivery and coordination of care for patients with SCD, facilitate approval of new medical products, and expand research on SCD. The post-marketing requirement for further study of Ferriprox aligns with the goals of the SCD Initiative.

The safety and effectiveness of Ferriprox is based on an analysis of data from twelve clinical studies in 236 patients. Patients participating in the study did not respond to prior iron chelation therapy. Ferriprox was considered a successful treatment for patients who experienced at least a 20 percent decrease in serum ferritin, a protein that stores iron in the body for later use. Half of the patients in the study experienced at least a 20 percent decrease in ferritin levels.

The most common side effects seen in patients who received Ferriprox included nausea, vomiting, abdominal and joint pain, urine chromaturia, neutropenia, and an increase in the level of a liver enzyme that may be indicative of tissue or liver damage at unsafe amounts.

The most serious side effect seen in about two percent of patients treated with Ferriprox was the development of agranulocytosis, a serious and potentially life-threatening reduction in the number of granulocytes (a type of white blood cell that fights infection).