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THE
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Cancer research news for clinicians

Chronic Myeloid Leukemia

Switching to Tasigna After Gleevec Therapy Can Achieve Deeper Molecular Response

Results from two phase III trials demonstrated the benefits of therapy with Tasigna compared to Gleevec tablets in the treatment of Philadelphia chromosome-positive chronic myeloid leukemia in newly diagnosed patients, and in those with residual disease who switched to Tasigna after long-term treatment with Gleevec.

Two-year results from the first study, ENESTcmr, showed that switching to Tasigna (nilotinib) led to deeper molecular responses in patients who still had evidence of residual disease after long-term therapy with Gleevec (imatinib mesylate).

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Breast Cancer

Perjeta, Herceptin & Docetaxel Combination Extended Survival in HER2-Positive Disease

Updated survival results from the phase III CLEOPATRA study showed that a combination of Perjeta (pertuzumab), Herceptin (trastuzumab) and docetaxel chemotherapy significantly extended overall survival of people with previously untreated HER2-positive metastatic breast cancer, compared to Herceptin, chemotherapy and placebo.

At the time of the analysis, median overall survival had not yet been reached in people receiving the Perjeta combination, as more than half of these people continued to survive. Median overall survival was 37.6 months for people who received Herceptin and chemotherapy. Results showed that the risk of death was reduced by 34 percent (HR=0.66; p=0.0008).

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Colorectal Cancer and GIST

Two Regorafenib Trials Demonstrate Efficacy, Improve Overall and Progression-Free Survival

Two phase III trials, CORRECT and GRID, demonstrated evidence for the efficacy of regorafenib in patients with metastatic colorectal cancer or gastrointestinal stromal tumors who have exhausted all other treatment options.

In CORRECT, regorafenib plus best supportive care significantly improved overall survival (HR=0.77, 1-sided p-value=0.0052) and progression-free survival (HR=0.49, 1-sided p-value <0.000001) compared to placebo plus BSC in patients with mCRC whose disease had progressed after approved standard therapies.

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

Tasigna Achieves Three Times The Early Response of Gleevec

(Continued from page 1)

More than twice as many patients treated with Tasigna continued to achieve undetectable BCR-ABL versus Gleevec. The difference between groups by 24 months was statistically significant (22.1 vs. 8.7 percent; p=0.0087) and that difference has doubled since the 12-month analysis.

Significantly more patients treated with Tasigna achieved MR4.5 or undetectable BCR-ABL versus Gleevec regardless of the BCR-ABL transcript level at baseline. In studies published to date, no patients achieving and maintaining MR4.5 have progressed to advanced stages of CML.

In the second study, ENESTnd, a four-year landmark analysis showed that more than three times as many patients achieved early molecular response (reduction in BCR-ABL transcript levels to 10 percent or less at months three and six) with Tasigna as frontline therapy instead of Gleevec.

The investigators correlated early molecular response with future major molecular response and MR4.5, as well as an increased probability of progression-free survival and overall survival.

In a separate four-year analysis of efficacy and safety data from ENESTnd, the difference in the rates of both MR4 and MR4.5 continued to be significantly higher for Tasigna, with the difference in favor of Tasigna increasing over time (MR4: 9-14 percent difference by one year, 17-24 percent difference by four years; MR4.5: 6-10 percent difference by one year, 14-17 percent difference by four years).

Overall survival remained similar in all groups at four years, but fewer CML-related deaths occurred in both the Tasigna 300 mg twice daily (n=5) and 400 mg twice daily (n=4) arms versus Gleevec (n=13).

Findings from both studies were presented at the annual meeting of the American Society of Hematology.

ENESTcmr is an open-label, randomized, prospective, multi-center study of Tasigna 400 mg twice daily versus standard-dose Gleevec, comparing kinetics of molecular response for patients with Ph+ CML in chronic phase who had achieved complete cytogenetic response but were still BCR-ABL positive after at least two years of treatment with Gleevec. The study enrolled 207 patients.

The primary endpoint was the rate of confirmed best complete molecular response by 12 months of study therapy with Tasigna or Gleevec. Secondary objectives included the kinetics of molecular response, duration of molecular response, progression-free survival and overall survival in both arms.

ENESTnd is a randomized, open-label, multicenter trial comparing the efficacy and safety of Tasigna versus Gleevec in adult patients with newly diagnosed Ph+ CML in chronic phase. It is the largest global randomized comparison of two oral therapies ever conducted in newly diagnosed Ph+ CML patients. The study is being conducted at 217 global sites with 846 patients enrolled.

Patients were randomized to receive Tasigna 300 mg twice daily (n=282), Tasigna 400 mg twice daily (n=281) or Gleevec 400 mg once daily (n=283). The primary endpoint was major molecular response at 12 months; the key secondary endpoint was durable MMR at 24 months. MMR was defined in this study as 0.1 percent or less of BCR-ABL as measured by RQ-PCR.

Both drugs were well tolerated. Few new adverse events and laboratory abnormalities were observed between two and three years. Rates of discontinuation due to AEs were 10 percent, 14 percent, and 11 percent in the Tasigna 300 mg BID, Tasigna 400 mg BID, and Gleevec arms, respectively.

Patients on the Gleevec treatment arm who had suboptimal response or treatment failure were allowed to escalate dose and/or switch to Tasigna in a separate extension study.

Tasigna is approved for the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia.

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Editor and Publisher: Paul Goldberg
Associate Editor: Conor Hale

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

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Tasigna is also approved in more than 90 countries for the treatment of chronic phase and accelerated phase Ph+ CML in adult patients resistant or intolerant to at least one prior therapy, including Gleevec. Tasigna is marketed by Novartis.

Acute Myeloid Leukemia

Volasertib Shows Response In 31 Percent of Acute Myeloid Leukemia Patients

Preliminary results from the phase II part of a phase I/II study of newly diagnosed acute myeloid leukemia patients who are considered ineligible for intensive remission induction therapy demonstrated higher rates of objective response, and a trend for longer median event free survival, when treated with the investigational compound volasertib in combination with low-dose cytarabine, compared to cytarabine treatment alone.

Volasertib is an investigational inhibitor of polo-like kinase (Plk1), an enzyme that regulates cell division. These results, presented at the annual meeting of the American Society of Hematology, support the initiation of a phase III study of volasertib in combination with LDAC.

The open-label study enrolled 87 adult patients randomly assigned to receive either volasertib in combination with LDAC (n=42) or LDAC alone (n=45). The primary endpoint was objective response—complete remission or CR with incomplete blood count recovery.

Objective responses were observed in 31 percent of patients (n=13) treated with the combination of volasertib plus LDAC compared with 13.3 percent of the patients (n=6) treated with LDAC alone (odds ratio: 2.91; p = 0.0523). The median time to remission was 71 days and 64 days, respectively.

Secondary endpoints included event-free survival, overall survival and safety. EFS was measured from the date of randomization to the date of disease progression, relapse or death from any cause, whichever occurred first.

In patients treated with the combination of volasertib plus LDAC, the median EFS was approximately 5.6 months compared with approximately 2.3 months in patients treated with LDAC alone (HR: 0.56; 95% CI: 0.34, 0.93; p=0.0237). Follow-up for overall survival was ongoing at the time of this analysis.

The drug's sponsor, Boehringer Ingelheim, intends to begin recruitment of a phase III study (NCT01721876) to assess the efficacy and safety of volasertib in combination with LDAC compared with LDAC alone in early 2013. The planned Phase III trial, POLO-AML-2, will enroll eligible patients aged 65 or older with previously untreated AML who are ineligible for intensive remission induction therapy.

The safety and efficacy of volasertib have not been established and it has not been approved by the FDA.

Breast Cancer

Perjeta, Herceptin & Docetaxel Reduce Risk of Progression 38%

(Continued from page 1)

Based on these data, people receiving Herceptin and chemotherapy in the study have been offered the option to receive Perjeta. No new safety signals were observed in the study.

People who received the combination of Perjeta, Herceptin and chemotherapy had a statistically significant 38 percent reduction in the risk of their disease worsening or death (PFS, HR=0.62, p-value=<0.0001) compared to people who received Herceptin, chemotherapy and placebo.

The median PFS improved by 6.1 months from 12.4 months for people who received Herceptin and chemotherapy to 18.5 months for those who received Perjeta, Herceptin and chemotherapy.

Perjeta is a personalised medicine that targets the HER2 receptor, a protein found in high quantities on the outside of cancer cells in HER2-positive cancers. Perjeta is believed to work in a way that is complementary to Herceptin, as the two medicines target different places on the HER2 receptor.

In June 2012, the FDA approved Perjeta in combination with Herceptin and docetaxel chemotherapy for the treatment of people with HER2-positive mBC, who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease, based on the results of the CLEOPATRA study. Perjeta's sponsor, Roche, has submitted an application to the European Medicines Agency for Perjeta for people with previously untreated HER2-positive metastatic breast cancer.

These data were presented at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium.

Breast Cancer Risk Increases With Repeated CT Imaging

Researchers reviewing the records of approximately 250,000 women enrolled in an integrated healthcare delivery system found that increased CT utilization between 2000 and 2010 could result in an increase in the risk of breast cancer for certain women, including younger patients and those who received repeat exams.

According to the study, nuclear medicine examinations may also contribute to increased breast cancer risk. The study was presented at the annual meeting of the Radiological Society of North America.

The study found that among the Northwestern Memorial Hospital system's female enrollees, CT utilization increased from 99.8 CT scans per 1,000 women in 2000 to 192.4 CT scans per 1,000 women in 2010—an annual increase of 6.8 percent.

In 2010, 46 percent of those CT examinations exposed the breast to radiation. Nuclear medicine imaging decreased from 39.3 scans per 1,000 women in 2000 to 27.5 scans per 1,000 women in 2010, a 3.5 percent annual decline; however, in 2010, 84 percent of nuclear medicine studies exposed the breast to radiation.

The research team collected dose information from 1,656 patients who underwent CT examinations that exposed the breast to radiation and estimated the patients' effective radiation dose and the amount of radiation absorbed by the breast. The team also analyzed the radiopharmaceutical volume and associated radiation exposure used in 5,507 nuclear medicine exams that exposed the breast to radiation.

The highest doses came from multiple-phase cardiac and chest CT examinations, where successive images of the organ are captured, according to researchers.

Each woman's 10-year imaging-related risk of developing breast cancer was estimated using the breast-specific radiation data and a statistical risk model. A women's underlying risk of developing breast cancer was estimated based on data collected by the NCI-funded Breast Cancer Surveillance Consortium.

"Young women receiving several chest and or cardiac CTs had the greatest increased risk of developing breast cancer at approximately 20 percent," said Diana Miglioretti, study coauthor and senior investigator at the Group Health Research Institute. "A 15-year-old girl with no risk factors for breast cancer would double her 10-year risk of developing breast cancer at 25."

Scatter Radiation from Mammography Presents No Increased Cancer Risk

The radiation dose to areas of the body near the breast during mammography is negligible, or very low, and does not result in an increased risk of cancer, according to a study. The results suggest that the use of thyroid shields during mammography is unnecessary.

Researchers set out to measure the dose received by the thyroid gland, salivary gland, sternum, uterus and the lens of the eye during screening digital mammography. Each of the 207 women in the study group wore six optically stimulated luminescent dosimeters while undergoing two-view screening mammography.

Analysis of the dosimeters by a medical physicist immediately after the exam revealed that the doses to the various areas outside of the breast ranged from negligible to very low.

The average estimated organ dose to both the salivary and thyroid glands was 0.05 mGy. These doses are only a fraction of the radiation people are exposed to from natural background sources. All areas except for the sternum received less than 2 percent of annual background radiation dose.

The study's results were presented at the annual meeting of the Radiological Society of North America.

Measured dose to the bridge of the eye and umbilicus was negligible, indicating no increased risk to the patient of cataracts or interference with normal embryonic development in early pregnancy.

The number of thyroid cancer diagnoses in women nearly doubled from 2000 to 2008, leading some to suspect that mammography may be a contributing factor and that women should wear lead thyroid shields during exams.

Based on the extremely low scatter radiation dose, thyroid shields are unnecessary during mammography. In addition, the researchers warn that use of thyroid shields could result in an increased radiation dose to patients by possibly causing repeat exams.

Colorectal Cancer and GIST

Regorafenib Extends Survival In Two Phase III Clinical Trials

(Continued from page 1)

Median OS was 6.4 months with regorafenib compared to 5.0 months with placebo; and median PFS was 1.9 months versus 1.7 months. The data also showed a survival benefit in the regorafenib arm across nearly all analyzed subgroups, including no significant difference between patients with KRAS wild-type tumor and those with KRAS mutant tumor. No difference in overall response rate was observed.

In GRID, regorafenib plus BSC significantly improved PFS compared to placebo plus BSC (HR=0.27, $p<0.000001$) in patients with metastatic and/or unresectable GIST who were previously treated with imatinib and sunitinib, with a 73 percent reduction in the risk of progression or death.

The median PFS was 4.8 months in the regorafenib arm compared to 0.9 months in the placebo arm. There was a positive trend in the regorafenib group in improving OS (HR=0.772, p=0.199); however, the OS did not reach statistical significance which was expected due to the cross-over design of the trial that allowed patients receiving placebo to receive regorafenib following disease progression.

Furthermore, a significantly greater disease control rate was observed with regorafenib plus BSC compared to placebo plus BSC (52.6 vs. 9.1 percent; $p<0.000001$), DCR was defined as rate of complete response plus partial response plus durable stable disease maintained for at least 12 weeks.

Regorafenib also demonstrated therapeutic benefit independent of prior treatment options based on analysis in pre specified subgroups that showed regorafenib had a statistically significant PFS benefit over placebo for patients receiving regorafenib as a third- or fourth-line treatment.

Both trials were published in The Lancet.

Regorafenib is an oral multi-kinase inhibitor that inhibits various kinases that are involved in mechanisms associated with oncogenesis, angiogenesis, and the tumor microenvironment.

Regorafenib was approved by the FDA for the treatment of mCRC and is marketed as Stivarga and has received priority review for treatment in GIST. Its sponsor, Bayer HealthCare, submitted an application for marketing approval of regorafenib for the treatment of mCRC in the EU in May 2012.

Prostate Cancer

MRI, 3D Ultrasound Combination Can Guide Prostate Biopsies

Research by a team of physicians and engineers at UCLA demonstrated that prostate cancer can be diagnosed using image-guided targeted biopsy.

Traditionally found only by blind biopsy, prostate cancer now appears detectable by direct sampling of tumor spots found using MRI in combination with real-time ultrasound, according to a study released early online for the January 2013 issue of The Journal of Urology.

The study showed that the MRI and ultrasound fusion biopsy may lead to a reduction in the numbers of prostate biopsies performed and allow for early detection of serious prostate cancers.

The study involved 171 men who were using active surveillance to monitor slow growing prostate cancers or men who had persistently elevated prostate specific antigen, but had prior negative biopsies. The biopsies were done in about 20 minutes in an outpatient clinic setting under local anesthesia.

Patients underwent MRI first to visualize the prostate and any lesions. That information is then fused with real-time, three-dimensional ultrasound.

Prostate cancer was found in 53 percent of 171 study participants. Of those tumors found by the fusion biopsy technique, 38 percent had a Gleason score of greater than seven.

Lymphoma

Perifosine, Sorafenib Combination Well Tolerated in Several Lymphomas

Final phase II data showed that a combination of perifosine and sorafenib was well tolerated by heavily pretreated patients with relapsed/refractory lymphomas. Promising clinical response activity was observed in patients with classical Hodgkin Lymphoma, suggesting that this subgroup could represent the target population for future studies.

Data were presented at the annual meeting of the American Society of Hematology.

The study involved 40 patients with relapsed/refractory lymphomas who had failed second or subsequent-line salvage chemotherapy, including: three patients with diffuse large B-cell lymphoma, three with follicular lymphoma, one with Waldenstrom

macroglobulinemia, eight with chronic lymphocytic leukemia and 25 with classical Hodgkin lymphoma. Twelve patients had relapsed and 28 patients had refractory disease.

The treatment plan included an initial four-week treatment with perifosine (50 mg BID, per os) to assess tolerability and tumor response. Subsequently, patients achieving less than partial response were given perifosine (50 mg BID, per os) combined with sorafenib (400 mg BID, per os) until progression of disease or significant clinical toxicity.

Patients achieving at least a partial response went off-study and continued with perifosine (50 mg BID, per os) alone until disease progression or clinical toxicity. Tumor response was assessed according to the revised response criteria for malignant lymphoma of the International Working Group.

Based on tumor response to the initial perifosine therapy, 36 of 40 patients who achieved less than PR were subsequently administered the perifosine/sorafenib combination therapy.

The median duration of combination therapy was 4 months (range: 2-18). For the 36 patients treated with combination therapy, eight had a partial response (22 percent), 15 showed stable disease (42 percent), and disease progressed in 13 patients (36 percent).

Median overall survival and progression free survival for all patients were 16 and 5 months, respectively.

For the 25 patients in the HL subgroup also receiving combination therapy, the overall response-rate was 28 percent, with 7 partial responses; for HL patients, median OS and PFS were 16 and 5 months respectively, as it was for all patients.

A significant correlation between pErk and pAkt reduction during the first 2 months of therapy and clinical response was demonstrated by logistic regression model. The reduction of pErk and pAkt values was related to a highly significant probability to observe a clinical response ($p=0.0003$ and $p=0.005$ for pErk and pAkt, respectively).

Perifosine is an oral anticancer treatment that inhibits Akt activation in the phosphoinositide 3-kinase (PI3K) pathway. It has been granted an Fast Track and orphan drug designations for multiple myeloma by the FDA. The drug is sponsored by Aeterna Zentaris Inc.

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NCI-Approved CTEP Trials For the Month of December

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

Phase I

9153: Phase I Study of Tivantinib Plus Bevacizumab. University of Pittsburgh; Appleman, Leonard Joseph. (412) 648-6507

9182: A Phase I Trial of the Combination of the PARP Inhibitor ABT-888 with Intraperitoneal Floxuridine (FUDR) in Epithelial Ovarian, Primary Peritoneal and Fallopian Tube Cancers. Mayo Clinic; Wahner Hendrickson, Andrea E. (507) 284-4430

9197: A Phase I Study of Ipilimumab in Combination with Rituximab in Patients with Relapsed/ Refractory CD20+ B-Cell Lymphoma. City of Hope; Tuscano, Joseph M. (916) 734-3771

9358: Transfer of Genetically Engineered Lymphocytes in Melanoma Patients: A Phase 1 Dose Escalation Study. Loyola University Medical Center; Clark, Joseph I. (708) 327-3236

Phase II

9312: Phase II Study of Cabozantinib in Patients with Radioiodine-Refractory Differentiated Thyroid Cancer Who Progressed on First-Line VEGFR-Targeted Therapy. Ohio State University Medical Center; Shah, Manisha H. (614) 293-8629

Phase III

E1A11: Randomized Phase III Trial of Bortezomib, Lenalidomide and Dexamethasone (VRd) Versus Carfilzomib, Lenalidomide, Dexamethasone (CRd) Followed by Limited or Indefinite Lenalidomide Maintenance in Patients with Newly Diagnosed Symptomatic Multiple Myeloma. Eastern Cooperative Oncology Group; Kumar, Shaji K. (507) 266-0523

S1216: A Phase III Randomized Trial Comparing Androgen Deprivation Therapy + TAK-700 with Androgen Deprivation Therapy + Bicalutamide in Patients with Newly Diagnosed Metastatic Hormone Sensitive Prostate Cancer. Southwest Oncology Group; Agarwal, Neeraj (901) 414-1779

AAML12B13: Development of Highly Sensitive Nano-Immunoassays to Define Aberrant Signaling and Test Pre-Clinical Therapeutics Targeting FLT3-ITD Positive Acute Myeloid Leukemia (AML). Children's Oncology Group; Sabnis, Himalee Shreekant. (404) 785-6194

AEPI10N5: Genetic Epidemiology of Ewing's Sarcoma. Children's Oncology Group; Schiffman, Joshua David. (801) 587-4745

AHOD13B1: 3D Telomere Structure as a Biomarker in Hodgkin Lymphoma. Children's Oncology Group; Wall, Donna A. (204) 787-7095

E2496T2: Prognostic Power of HGAL (GCET2) Protein Expression in Classical Hodgkin Lymphoma: A Proposal for Evaluation in the E2496 Study. Eastern Cooperative Oncology Group; Lossos, Izidore. (305) 243-4785

NCIC-MA.27E-MAYO-ICSC: A Genome-Wide Association Study in Patients Experiencing Breast Events While Receiving Aromatase Inhibitors for Early Breast Cancer on NCIC CTG Trial MA.27. National Cancer Institute of Canada Clinical Trials Group; Ingle, James N. (507) 284-4798

Pilot Phase

ANBL12P1: Pilot Study Using Myeloablative Busulfan/Melphalan (BuMel) Consolidation Following Induction Chemotherapy for Patients with Newly Diagnosed High-Risk Neuroblastoma. Children's Oncology Group; Granger, Mary Meaghan Petty. (682) 885-2580

FDA Approvals

FDA Approves 35 Medicines In Fiscal 2012, Eight in Cancer

The FDA approved 35 novel medicines in the 2012 fiscal year, including the first drugs to treat advanced basal cell carcinoma, among a total of eight drugs to treat cancer.

The approvals are detailed in the agency's report, "FY 2012 Innovative Drug Approvals." The number of approvals matches the agency's performance in FY 2011.

This year's approvals include a novel treatment for a form of cystic fibrosis, the first human cord blood product ever approved, new therapies in HIV and macular degeneration, as well as two approvals in personalized medicine and nine new drugs for orphan diseases.

Seventy-seven percent of the drugs were approved on their first cycle of review, and 34 out of the 35 met their target approval dates under the Prescription Drug User Fee Act. The FDA had expedited the review process of over half of these medicines using its fast track, priority review and accelerated approval methods.

The eight drugs approved in cancer-related indications are:

- **Erivedge (vismodegib)**, approved in 4.7 months for metastatic basal cell cancer
- **Xtandi (enzalutamide)**, approved in 3.3 months for late-stage prostate cancer
- **Jakafi (ruxolitinib)**, approved in 5.5 months for myelofibrosis
- **Voraxaze (glucarpidase)**, approved in 6 months to lower toxic levels of the chemotherapy drug methotrexate
- **Erwinaze (asparaginase erwinia chrysthemi)**, approved in 12.6 months for acute leukemia
- **Stivarga (reborafenib)**, approved in 5.0 months for late-stage colorectal cancer
- **Perjeta (pertuzumab)**, approved in 6.0 months for late-stage breast cancer
- **Bosulif (bosutinib)**, approved in 9.6 months for chronic leukemia

The full report can be downloaded here: http://1.usa.gov/u7fC4E.

FDA approved Iclusig (ponatinib) for the treatment of adults with chronic myeloid leukemia and Philadelphia chromosome positive acute lymphoblastic leukemia, under the agency's accelerated approval program.

Iclusig blocks certain proteins that promote the development of cancerous cells. The drug is taken once a day to treat patients with chronic, accelerated, and blast phases of CML and Ph+ ALL whose leukemia is resistant or intolerant to a class of drugs called tyrosine kinase inhibitors.

Iclusig targets CML cells that have a particular mutation, known as T315I, which makes these cells resistant to currently approved TKIs.

Iclusig's safety and effectiveness were evaluated in a single clinical trial of 449 patients with various phases of CML and Ph+ ALL. All participants were treated with Iclusig.

The drug's effectiveness was demonstrated by a reduction in the percentage of cells expressing the Philadelphia chromosome genetic mutation found in most CML patients, or major cytogenetic response. Fifty-four percent of all patients and 70 percent of patients with the T315I mutation achieved the response. The median duration had not yet been reached at the time of analysis.

In accelerated and blast phase CML and Ph+ ALL, Iclusig's effectiveness was determined by the number of patients who experienced a normalization of white blood cell counts or had major hematologic response.

Results showed that 52 percent of patients with accelerated phase CML experienced MaHR for a median duration of 9.5 months; 31 percent of patients with blast phase CML achieved MaHR for a median duration of 4.7 months; and 41 percent of patients with Ph+ ALL achieved MaHR for a median duration of 3.2 months.

Iclusig is being approved with a Boxed Warning alerting patients and health care professionals that the drug can cause blood clots and liver toxicity. The most common side effects reported during clinical trials include high blood pressure, rash, abdominal pain, fatigue, headache, dry skin, constipation, fever, joint pain, and nausea.

Iclusig is marketed by ARIAD Pharmaceuticals.

FDA expanded the approved use of Zytiga (abiraterone acetate) to treat men with metastatic, castration-resistant prostate cancer prior to receiving chemotherapy.

The FDA initially approved Zytiga in November 2011 for use in patients whose prostate cancer progressed after treatment with docetaxel.

Zytiga's safety and effectiveness for its expanded use were established in a clinical study of 1,088 men with metastatic, castration-resistant prostate cancer who had not previously received chemotherapy. Participants received either Zytiga or a placebo in combination with prednisone. The study was designed to measure overall survival and radiographic progression-free survival.

Patients who received Zytiga had a median overall survival of 35.3 months compared with 30.1 months for those receiving the placebo. Study results also showed Zytiga improved rPFS. The median rPFS was 8.3 months in the placebo group and had not yet been reached for patients treated with Zytiga at the time of analysis.

The most common side effects reported in those receiving Zytiga include fatigue, joint swelling or discomfort, swelling caused by fluid retention, hot flush, diarrhea, vomiting, cough, high blood pressure, shortness of breath, urinary tract infection, and bruising.

The most common laboratory abnormalities included low red blood cell count; high levels of the enzyme alkaline phosphatase, which can be a sign of other serious medical problems; high levels of fatty acids, sugar, and liver enzymes in the blood; and low levels of lymphocytes, phosphorous and potassium in the blood.

Zytiga is marketed by Janssen Biotech Inc.

The European Commission approved expanding the label of Thyrogen (thyrotropin alfa) with a wider irradiation dose range for postoperative thyroid remnant ablation.

Thyrogen is used before radioiodine treatment to avoid temporarily discontinuing thyroid replacement therapy for postoperative thyroid remnant ablation.

The revised indication in remnant ablation provides physicians with the option to administer a reduced dose of radioiodine. Previously the amount of radioiodine was specified at 100 mCi, whereas physicians may now select a dose from the range of 30 to 100 mCi.

The decision to approve the expanded indication for use of Thyrogen in Europe is based on the results of the two largest studies (HiLo and ESTIMABL) ever conducted in thyroid remnant ablation. The studies, published in the New England Journal of Medicine in May 2012, evaluated whether rates of successful ablation would be similar among patients receiving recombinant human thyrotropin, patients undergoing thyroid hormone withdrawal, and among patients receiving low or high amount of radioiodine.

In the two studies, a dose of 30 mCi of radioiodine was well tolerated and showed similar success rates for low-dose radioiodine plus rhTSH vs. high-dose plus THW or rhTSH. In both studies, patients receiving Thyrogen rather than THW had fewer hypothyroid symptoms and better preserved quality of life.

Thyrogen is marketed by Genzyme, a Sanofi company.