The Clinical Cancer Letter

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Pancreatic Cancer

Abraxane-Gemcitabine Combination Extends Overall Survival in Phase III Trial

A phase III trial of Abraxane extended overall survival in metastatic pancreatic cancer, with some patients surviving longer than three years, when used in combination with gemcitabine.

The updated OS data from the Metastatic Pancreatic Adenocarcinoma Clinical Trial was presented at the American Society of Clinical Oncology Gastrointestinal Conference in San Francisco.

According to researchers, 4 percent of patients taking Abraxane (nanoparticle albumin-bound paclitaxel) and gemcitabine were alive after three years, compared to zero patients in the gemcitabine-alone arm.

(Continued to page 2)

Leukemia

Phase III Trial of Imbruvica Halted, Following Increases in Progression-Free Survival

A phase III study of Imbruvica in the treatment of chronic lymphocytic leukemia and small lymphocytic lymphoma was stopped early following an interim analysis and at the recommendation of an independent data monitoring committee, which concluded the study demonstrated a significant difference in progression-free survival compared to ofatumumab.

The IDMC agreed that the results suggest evidence of clinical benefit, as well as a tolerable safety profile. The committee also recommended that the drug's sponsor provide access to Imbruvica (ibrutinib) to patients in the ofatumumab arm.

Study PCYC-1112-CA (RESONATE) is an international, randomized, open-label clinical study including 391 patients with relapsed or refractory CLL/SLL with measurable nodal disease and who were not eligible for treatment with purine analog-based therapy, who had received at least one prior therapy.

(Continued to page 3)

Breast Cancer

Long-term Follow-up Shows ADH and ALH Tissue Abnormalities Can Carry Similar Risk

Contrary to existing understanding, long-term follow-up of patients with two types of breast tissue abnormalities suggests that both types of abnormalities have the same potential to progress to breast cancer.

The study, published in Cancer Prevention Research, a journal of the American Association for Cancer Research, challenges current understanding that atypical ductal hyperplasia leads to breast cancer in the same breast, while atypical lobular hyperplasia may not be a direct precursor of breast cancer, but may indicate equal risk of breast cancer across both breasts.

(Continued to page 4)

Kidney Cancer
Study Shows Patients Taking Hypertension Medication Lived Longer
. . . Page 2

Prostate Cancer
Five-Gene Assay Can Provide Valid Prognostic Information, Study Says
. . . Page 4

Colon Cancer
OncotypeDX Studies Presented at ASCO GI Cancer Symposium
. . . Page 4

Lung Cancer
Study: MicroRNA Assay Detects Lung Cancer Two Years Before LDCT
. . . Page 5

NCI-Approved Trials
. . . Page 5

FDA News
Accelerated Approval Granted to Mekinist-Tafinlar Combination
. . . Page 6

Abraxane Increases OS In Phase III Clinical Trial

(Continued from page 1)

The median survival benefit in the updated analysis was extended in the combination arm with a 2.1 month improvement in OS compared to gemcitabine alone (median 8.7 months vs. 6.6 months; HR=0.72; p<0.0001). This compares favorably with the 1.8 months improvement previously reported in the New England Journal of Medicine (median 8.5 months vs. 6.7 months; HR=0.72; p<0.00001).

The MPACT study was an open-label, randomized, international study of 861 patients with metastatic pancreatic cancer. Patients were randomized to receive either Abraxane plus gemcitabine (125 mg/m(2) followed by 1000 mg/m(2) gemcitabine for 3 weeks followed by a week of rest) or gemcitabine alone (1000 mg/m(2) administered weekly for 7 weeks followed by a week of rest followed by cycles of weekly administration for 3 weeks followed by one week of rest).

The primary endpoint for the study was overall survival. Secondary endpoints were progression-free survival and overall response rate determined by independent radiological review. Other endpoints included progression-free survival and overall response rate determined by investigator, and the safety and tolerability of this combination in this patient population.

Abraxane is approved for metastatic breast cancer in over 40 countries including the U.S., the European Union, Japan, and China, and is currently in various stages of investigation for the treatment of metastatic melanoma, adjuvant pancreatic cancer, bladder cancer, ovarian cancer, and expanded applications for breast cancer.

Abraxane combines paclitaxel with albumin, a naturally-occurring human protein, to deliver the drug and eliminates the need for solvents in the administration process. Nanoparticle technology allows it to deliver a 49 percent higher dose compared to regular solvent-based paclitaxel without compromising safety and tolerability. Abraxane is a registered trademark of Celgene Corporation.

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Kidney Cancer

Patients on Hypertension Meds Lived Longer, Analysis Shows

Patients with advanced kidney cancer lived an average of seven months longer if they were taking a common type of high blood pressure medication during treatment, according to an analysis of clinical trials data.

Patients on angiotensin system inhibitors, including angiotensin-converting-enzyme inhibitor and angiotensin system blockers, survived an average of 26.68 months compared with 17.05 months in those who did not receive the drugs.

The study results will be presented Feb. 1 at the 2014 ASCO Genitourinary Cancers Symposium in San Francisco.

The greatest survival benefits were seen in patients who were taking ASIs while being treated with drugs that targeted the vascular endothelial growth factor pathway, according to the study.

Researchers used a database of results of phase II and III clinical trials sponsored by Pfizer Inc. The pooled data included 4,736 patients treated between 2003 and 2013 for metastatic kidney cancer. The patients were generally males, younger than 65, whose disease was considered intermediate-risk.

The majority were treated with the targeted anti-VEGF agents sunitinib, sorafenib, and axitinib. Others received temsirolimus, which inhibits the mTOR protein, and interferon, which stimulates the immune system to fight tumors. Survival gains were greatest in patients who took ASIs while in treatment with anti-VEGF drugs, compared with mTOR inhibitors or interferon, the analysis revealed.

"Though larger prospective studies are needed to further investigate this hypothesis, based on the results of this study, an ASI should be considered for patients

with metastatic renal cell carcinoma who need an antihypertensive and do not have any contraindications that preclude their use, especially in patients receiving VEGF-targeted treatments," said Rana McKay, a clinical oncology fellow at Dana-Farber Cancer Institute. She cautioned it is too early to recommend ASIs for kidney cancer patients who don't need an antihypertension drug.

Toni Choueiri, clinical director of the Lank Center for Genitourinary Oncology at Dana-Farber and director of the kidney cancer center at Dana-Farber is senior author of the report. Other authors are from Rutgers University and Pfizer Oncology. The research was supported by Pfizer.

Leukemia

Phase III Imbruvica Trial Stopped Following Interim Analysis

(Continued from page 1)

Patients were randomized to receive 420 mg of Imbruvica orally once daily or intravenous doses of ofatumumab, an approved treatment for relapsed/refractory CLL, over the course of 24 weeks. Both treatments were administered until disease progression or unacceptable toxicity. The results will be presented at an upcoming medical meeting and also will be submitted for publication in a peer-reviewed journal.

Imbruvica was approved in November 2013 in the U.S. as a single agent for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy. This indication is based on overall response rate. An improvement in survival or disease-related symptoms has not been established.

Ibrutinib has been submitted to the European Medicines Agency for the treatment of adult patients with relapsed or CLL/SLL or adult patients with relapsed or refractory MCL. Ibrutinib is being jointly developed and commercialized by Janssen Research and Development and Pharmacyclics Inc. Pharmacyclics sponsored the study.

Liver Cancer

Post-Hoc Analysis of ThermoDox Suggests OS Improvement

A post-hoc analysis of results from the phase III HEAT Study of ThermoDox, a heat-activated liposomal encapsulation of doxorubicin in combination with radio frequency ablation, suggests the agent may significantly improve overall survival in primary liver cancer patients that receive RFA treatment for 45 minutes or more.

This analysis followed the announcement on January 31, 2013, that the HEAT Study did not meet its primary endpoint of progression-free survival.

As provided for in the HEAT Study's Special Protocol Assessment agreement with FDA, the drug's sponsor, Celsion Corporation, continues to follow patients for overall survival. Data from four quarterly reviews of overall survival have been evaluated since the announcement of top-line PFS data.

These findings apply to patients with single HCC lesions, 64.4 percent of the HEAT Study population, from both size cohorts of the HEAT Study (3-5 cm and 5-7 cm) and represent a subgroup of 285 patients, or 41 percent of the patients in the HEAT Study.

In the patient subgroup treated in the ThermoDox arm whose RFA procedure lasted longer than 45 minutes (n=285, or 63 percent of single lesion patients), clinical results indicate a 55 percent improvement in overall survival (HR=0.64; 95% CI: 0.41-1.00; p=0.0495). Median overall survival for this subgroup has not yet been reached.

In contrast, the patient subgroup treated with ThermoDox whose RFA procedure lasted less than 45 minutes in duration (n=167, or 37 percent of single lesion patients) indicated a Hazard Ratio of 1.12 (95% CI 0.68 - 1.86) and a P-value = 0.66. Median overall survival for this subgroup has not yet been reached.

The hazard ratios reported above warrant additional clinical development, and should be viewed with caution since they are based on a retrospective analysis and the HEAT Study has not reached its median point for overall survival analysis.

Celsion will continue to follow patients in the HEAT Study to the secondary endpoint, overall survival, and will update the subgroup analysis based on RFA heating duration. Celsion anticipates initiating a global phase III trial in the first half of 2014.

Breast Cancer

ADH, ALH Tissue Abnormalities Can Carry Similar Cancer Risk

(Continued from page 1)

"Ours is the first report with sufficient numbers of both types of atypia and long-term follow-up for breast cancers that compared the side of breast that had atypia with the side of breast in which cancer arose and the timeframe when the cancers developed," said Lynn Hartmann, professor of oncology at the Mayo Clinic. "We showed that even though the two types of atypia look different histologically, they behave quite similarly in terms of what happens to patients."

Hartmann and colleagues identified 698 women from the Mayo Benign Breast Disease Cohort who had biopsy-confirmed atypia; 330 of them had ADH, 327 had ALH, and 32 had both. The investigators followed these women for an average of 12.5 years, and 143 of them developed breast cancer.

The investigators found that the ratio of breast cancer in the same breast in which the atypia was detected versus in the opposite breast was the same, 2:1, for both ADH and ALH.

A similar number of women with either ADH or ALH developed breast cancer in the same breast within five years of diagnosis, which led the authors to suggest that, like ADH, ALH may also be a precursor in addition to being a risk indicator.

The study also found that ALH predominantly resulted in ductal cancer of the breast, which is a similar outcome as with ADH. Both ADH and ALH resulted in invasive ductal cancers, of which 69 percent were of intermediate- or high-grade. About 25 percent of them had spread to the lymph nodes. The pattern of cancers in these patients resembled those seen in the general population.

Prostate Cancer

Study: Gene Assay Can Provide Valid Prognostic Information

A study in aggressive prostate cancer confirmed that epigenetic profiling of selected genes can provide prognostic information corresponding to Gleason score.

"Men diagnosed with GS6 cancer may be eligible for active surveillance, however, today's standard 12-core transrectal ultrasound-guided biopsies are susceptible to under-sampling, leaving men at risk for undetected aggressive disease," noted E. David Crawford, professor of surgery and radiation oncology, and head of the Section of Urologic Oncology at the University of Colorado Denver School of Medicine.

The prognostic value of the epigenetic status of five genes—GSTP1, APC, RASSF1, RARB and LGALS3—in 84 prostatectomy samples with different GS's was evaluated. The results of a hierarchical clustering analysis showed that low gene methylation levels were detected in the vast majority of patient samples with GS6 and GS7 (3+4) PCa.

In contrast, respectively 81 percent and 91 percent of the GS7 (4+3) and GS $\geq$ 8 samples fell into the category with intermediate to high methylation levels. These data provide evidence of the potential prognostic value of the epigenetic profile of selected genes to identify men with a low versus high risk for aggressive PCa.

The study was presented at the 2014 ASCO Genitourinary Cancers Symposium 2014 in San Francisco. The genes are part of MDxHealth SA's ConfirmMDx for Prostate Cancer diagnostic, which detects an epigenetic field effect associated with the cancerization process at the DNA level.

Colon Cancer

Studies of Oncotype DX Test Presented at ASCO Symposium

A series of studies of the Oncotype DX colon cancer test were presented at the 2014 American Society of Clinical Oncology Gastrointestinal Cancer Symposium.

A review of four validation studies of the Oncotype DX colon cancer test, which included a total of 3,315 patients with early stage colon cancer, consistently demonstrated a significant association ($p<0.05$) between the test results and recurrence risk and cancer-specific survival.

Based on these results, the colon cancer test meets level I evidence criteria, according to the test's sponsor, Genomic Health Inc., and it underscores the test's clinical value beyond traditional clinicopathologic variables such as age, tumor size, tumor grade, number of nodes examined or evidence of lymphovascular invasion.

Additionally, three decision impact studies with a total of 502 patients showed that the test changed treatment recommendations in 29 to 45 percent of stage II colon cancer cases, leading to a net reduction in adjuvant chemotherapy use.

This analysis included previously-presented positive results by Partnership for Health Analytic

Research, a multi-center study conducted in collaboration with the Mayo Clinic Cancer Research Consortium and a study conducted by Clalit Health Services in Israel.

A separate prospective study, which analyzed physician recommendations and patient treatment preferences before and after receiving the Oncotype DX colon cancer test results, demonstrated that the test greatly increased concordance between physician and patient treatment choice, from 66 percent to 96 percent.

The evaluation showed that the quantitative information provided by the Recurrence Score result influenced a majority of patients' treatment decisions, 85 percent, and physicians' treatment recommendations, 69 percent, and it increased 84 percent of physicians' confidence in their own recommendations. Patients' anxiety was also significantly reduced.

Lung Cancer

MicroRNA Assay Detects Cancer Two Years Before LDCT in Study

Clinical validation study results of a microRNA signature classifier lung cancer assay demonstrated that a blood-based test can significantly reduce the high false-positive rate associated high-resolution imaging, specifically with low-dose computed tomography.

The MSC Lung Cancer assay, developed by Gensignia Ltd., detected lung cancer up to two years prior to diagnosis by LDCT.

Aspects of the study were presented as a plenary talk at the AACR-IASLC Molecular Origins of Lung Cancer meeting. The study was also published in the Journal of Clinical Oncology.

Prospectively collected blood samples from 939 heavy smokers from the randomized lung cancer screening trial comparing LDCT versus observation (Multicentric Italian Lung Detection trial) were used to validate the diagnostic performance and demonstrate clinical utility of the 24 microRNA expression signature assay.

Heavy smokers from the MILD trial that were cancer-free (n=870) or diagnosed with lung cancer (n=69) were examined in this correlative study. The assay demonstrated an overall sensitivity of 87 percent for the presence of lung cancer.

For all subjects, the assay had negative predictive values of 99 percent and 99.86 percent for detection and death-by-disease (lung cancer), respectively, indicating the test's high specificity for correctly identifying subjects without lung cancer.

The high specificity of the MSC Lung Cancer assay resulted in a five-fold reduction in the false positive rate of LDCT-identified suspicious lung nodules in heavy smokers that did not have lung cancer.

Gensignia intends to introduce a lung cancer diagnostic test in the U.S. in 2014.

NCI CTEP Approved Trials For the Month of January

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

9524: A Phase I Study of Pomalidomide Given at the Time of Lymphocyte Recovery Following Induction Timed Sequential Chemotherapy with Cytarabine, Daunorubicin and Etoposide (AcDVP16) in Patients with Newly Diagnosed Acute Myeloid Leukemia (AML) and High-Risk MDS. Johns Hopkins University; Gojo, Ivana. (410) 328-2596

Phase II

9539: A Randomized, Prospective, Phase II Study to Determine the Efficacy of Bacillus Calmette-Guerin (BCG) Given in Combination with PANVAC(TM) Versus BCG Given Alone in Adults with High Grade Non-Muscle Invasive Bladder Cancer (NMIBC) Who Failed at Least 1 Induction Course of BCG. National Cancer Institute Urologic Oncology Branch; Agarwal, Piyush K. (301) 496-6353

ACNS1221: A Phase II Study for the Treatment of Non-Metastatic Nodular Desmoplastic Medulloblastoma in Children Less Than 4 Years of Age. Children's Oncology Group; Lafay-Cousin, Lucie. (403) 955-2554

ACRIN-6702: A Multi-Center Study Evaluating the Utility of Diffusion Weighted Imaging for Detection and Diagnosis of Breast Cancer. American College of Radiology Imaging Network; Partridge, Savannah Corrina (206) 288-1306

E2212: A Randomized, Double-Blinded, Placebo-Controlled Phase II Study of Adjuvant Everolimus Following the Resection of Metastatic Pancreatic Neuroendocrine Tumors to the Liver. Eastern Cooperative Oncology Group; Libutti, Steven Kenneth. (718) 920-4231

S1310: Randomized Phase II Trial of Single Agent MEK Inhibitor Trametinib (GSK1120212) Vs 5-Fluorouracil or Capecitabine in Refractory Advanced Biliary Cancer. Southwest Oncology Group; Kim, Richard D. (813) 745-1277

Phase III

A091105: A Phase III, Double Blind, Randomized, Placebo-Controlled Trial of Sorafenib in Desmoid Tumors or Aggressive Fibromatosis (DT/DF). Cancer and Leukemia Group B; Gounder, Mrinal Murugesan. (646) 888-4167

Other Phases

AALL13B10-Q: Mechanisms of Action of Bortezomib in Early T-Precursor Acute Lymphoblastic Leukemia (ALL). Children's Oncology Group; Horton, Terzah M. (832) 824-4269

AALL13B11-Q: Translocations and Their Widespread Impact on Gene Regulation. Children's Oncology Group; Skok, Jane A. (212) 263-0504

AALL13B7-Q: Acute Lymphoblastic Leukemia Therapy By Targeting Cancer Stem Cells. Children's Oncology Group; Schore, Reuven Joshua. (202) 476-2800

ANBL13B8-Q: The Genetic Basis of Neuroblastoma Tumorigenesis. Children's Oncology Group; Maris, John M. (215) 590-5244

9510: Pilot Trial of BMN 673, an Oral PARP Inhibitor, in Patients with Advanced Solid Tumors and Deleterious BRCA Mutations. National Cancer Institute Developmental Therapeutics Clinic; Kummar, Shivaani. (301) 435-5402

CITN-05: A Pilot Study of the Immunological Effects of Neo-Adjuvant INCB024360 in Patients with Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma. Cancer Immunotherapy Trials Network; Odunsi, Kunle. (716) 845-8376

FDA News

FDA Grants Accelerated Approval To Mekinist-Tafinlar Combination

FDA granted accelerated approval for Mekinist (trametinib) in combination with Tafinlar (dabrafenib) for unresectable melanoma or metastatic melanoma with BRAF V600E or V600K mutations.

The approval was based on the demonstration of response rate and median duration of response in a phase I/II study, and is dependent on the results of an ongoing phase III trial (MEK115306 or Combi-D). The combination was reviewed under a Priority Review designation.

Improvement in disease-related symptoms or overall survival has not been demonstrated for Mekinist in combination with Tafinlar. The BRAF mutations must be detected by an FDA-approved test. Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma.

In the phase II portion of the open-label study, the main efficacy endpoint of overall response was 76 percent for patients treated with the combination (n=54; 95% CI, 62, 87), and 54 percent for patients treated with single-agent Tafinlar (n=54; 95% CI, 40, 67).

The median duration of response was 10.5 months for patients treated with the combination (95% CI, 7, 15), and 5.6 months for patients treated with single-agent Tafinlar (95% CI, 5, 7). When enrolling patients, no more than one prior chemotherapy regimen and/or interleukin-2 was permitted. Patients with prior exposure to BRAF inhibitors or MEK inhibitors were ineligible.

Mekinist and Tafinlar are both sponsored by GlaxoSmithKline.

FDA granted 510(k) to Royal Philips's Spectral Breast Density Measurement Application for its MicroDose SI full-field digital mammography system. The application is the first spectral breast density measurement tool, meaning adipose and glandular tissue can be differentiated to measure volumetric breast density.

The application measures the glandularity and thickness in each pixel of the image to objectively calculate the total volume and volumetric percentage of glandular tissue in the breast. Once the calculations are completed the examination is automatically assigned a MicroDose density score that correlates to the Breast Imaging-Reporting and Data System, the manual method for determining breast density.

The measurement is displayed on the review

workstation together in the DICOM tag of the acquired image, and exported for display in a DICOM structured report. The application of non-contrast spectral imaging is made possible by sorting photons into low- or high-energy categories, eliminating the need for two exposures.

FDA approved Miltenyi Biotec's CliniMACS CD34 Reagent System as a Humanitarian Use Device for the prevention of graft-versus-host disease in patients with acute myeloid leukemia in first complete remission undergoing allogeneic stem cell transplantation from a matched related donor.

The system removes donor T cells from the graft prior to transplantation by enriching CD34+ blood stem cells, which go on to repopulate the patient's immune and blood building systems.

Approval was based on data from a phase II, single-arm, multi-center study (BMT CTN 0303) conducted by the Blood and Marrow Transplant Clinical Trials Network.

The trial showed that following intensive myeloablative conditioning, stem cell transplantation from an identical sibling donor processed using the system as the sole means of GVHD prophylaxis lead to a low incidence of chronic GVHD (19 percent at two years after transplantation) without negatively affecting relapse, engraftment, overall survival or disease-free survival.

FDA launched the advisory committee membership nomination portal that allows individuals to submit nominations for membership to any of the agency's 33 advisory committees.

The portal allows applicants to complete their entire application online. Currently, applications must either be emailed or mailed to the agency.

Nominations for scientific members and consumer and industry representatives may be submitted by professional societies, industry and consumer groups, and other interested persons and organizations.

Potential candidates are asked to provide detailed information concerning such matters as financial holdings, employment, and research grants and/or contracts in order to permit evaluation of possible sources of conflict of interest.

In conjunction with the launch of the nomination portal, the FDA is also posting a set of presentation slides on conflicts of interest for potential members, which can help in answering preliminary questions.

FDA granted an Orphan Drug Designation to BL-8040, developed by BioLineRx, as a treatment for stem cell mobilization, in addition to the orphan designation previously granted to BL-8040 as a treatment for Acute Myeloid Leukemia.

The designation was granted for use of BL-8040 in combination with granulocyte colony-stimulating factor to mobilize human stem cells from the bone marrow to the peripheral blood for collection for autologous or allogeneic transplantation.

BL-8040 is a short peptide that functions as a high-affinity antagonist for CXCR4, a chemokine receptor that is directly involved in tumor progression, angiogenesis, metastasis and cell survival. CXCR4 is over-expressed in more than 70 percent of human cancers and its expression often correlates with disease severity. BL-8040 mobilizes cancer cells from the bone marrow and may therefore sensitize these cells to chemo- and bio-based anti-cancer therapy. Importantly, BL-8040 has also demonstrated a direct anti-cancer effect by inducing apoptosis.

FDA notified Cell Therapeutics Inc. that the partial clinical hold on tosedostat (IND 075503) has been removed and all studies underway may continue.

Tosedostat is an oral selective inhibitor of aminopeptidases, which provide amino acids necessary for growth and tumor cell survival, and is under development for the treatment of blood-related cancers.

Tosedostat is currently being studied in the U.S. and the European Union in investigator-sponsored and cooperative group-sponsored phase II trials in elderly patients with newly diagnosed and relapsed acute myeloid leukemia and high-risk myelodysplastic syndromes.

FDA and the European Medicines Agency launched a joint initiative to share information on inspections of bioequivalence studies submitted in support of generic drug approvals. This collaboration provides a mechanism to conduct joint facility inspections for generic drug applications submitted to both agencies.

France, Germany, Italy, the Netherlands, and the United Kingdom are also taking part in this initiative.

A key objective of the initiative is to streamline information sharing on inspections of bioequivalence studies conducted and planned for generic drug applications. Inspectional information will be shared for clinical facilities, analytical facilities, or both.

Information will be shared about negative

inspection outcomes that reveal system problems at a facility, joint inspections will be conducted at facilities all over the world, and training opportunities will be provided. This initiative will use confidentiality arrangements established among the European Commission, the EMA, interested EU member states, and the FDA.

The agreement includes an 18-month pilot phase and follows the 2009 EMA-FDA Good Clinical Practices Initiative.

The European Commission has amended the product information of Erbitux (cetuximab), updating the indication to include RAS wild-type metastatic colorectal cancer.

The approval follows the positive opinion from the Committee for Medicinal Products for Human Use issued in November 2013, and is based on the totality of data emerging on the role of mCRC RAS tumor status in the benefit-risk profile of the drug. The approval primarily refers to new biomarker data from the OPUS (OxaliPlatin and cetUximab in firSt-line treatment of mCRC) study.

In recent analyses of studies evaluating monoclonal anti-epidermal growth factor receptor antibodies, such as Erbitux, tumor samples of patients with KRAS wild-type tumor status (exon 2) were assessed for additional RAS mutations (defined as mutations in exons 3 or 4 of KRAS and/or exons 2, 3 or 4 of NRAS). The results from these studies suggest that patients with RAS wild-type tumors may benefit from treatment with Erbitux, while patients with RAS mutant tumors may not.

In the updated product information, Erbitux will now be indicated for the treatment of patients with EGFR-expressing, RAS wild-type mCRC in combination with irinotecan-based chemotherapy, in first-line in combination with FOLFOX, or as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan.

Erbitux is sponsored by Merck Serono, the biopharmaceutical division of Merck.

The EU Committee for Medicinal Products for Human Use has recommended approval of Roche's subcutaneous formulation of MabThera (rituximab) using Halozyme's recombinant human hyaluronidase (rHuPH20) for the treatment of patients with common forms of non-Hodgkin lymphoma.

Currently, MabThera is delivered by an intravenous infusion which takes approximately 2.5 hours. The new MabThera SC formulation comes as a ready-to-use, fixed dose, 1,400 mg solution.

The CHMP opinion is based primarily on data from Roche's phase III SABRINA study. Roche expects a final decision from the European Commission in the coming months.

The European Commission granted orphan drug status to Eisai's Amatuximab for the treatment of malignant mesothelioma.

Amatuximab is a chimeric immunoglobulin G-1-kappa (IgG1/kappa) monoclonal antibody with high affinity and specificity for mesothelin, a glycoprotein currently considered an important target of mesothelioma treatment, due to its overexpression on tumor cells.

Amatuximab was discovered and developed through Morphotek, a subsidiary of Eisai.

The National Institute for Health and Care Excellence in the U.K. issued a Final Appraisal Determination for Pixuvri (pixantrone), sponsored by Cell Therapeutics Inc

The positive draft guidance determines Pixuvri is cost effective and recommends funding the treatment as a monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive B-cell non-Hodgkin lymphoma, including diffuse large B-cell lymphoma.

The NICE Appraisal Committee recommended the treatment as an option for certain people with histologically confirmed aggressive B-cell NHL who have previously received rituximab and are receiving Pixuvri as a third- or fourth-line treatment.

The determination forms the basis of the final guidance to the NHS in England and Wales and is expected to be published in February 2014. Once the final guidance is published, the NHS must fully implement it within 90 days.

Pixuvri is an aza-anthracenedione that forms stable DNA adducts and in preclinical models. It is structurally designed so that it cannot bind iron and perpetuate oxygen radical production, or form a long-lived hydroxyl metabolite—both of which are the putative mechanisms for anthracycline induced acute and chronic cardiotoxicity.

In May 2012, the European Commission granted conditional marketing authorization for Pixuvri as a monotherapy for the treatment of adult patients with multiply relapsed or refractory aggressive NHL.