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Leukemia

Arzerra Maintenance Therapy Extends PFS In Phase III Trial, Compared to Observation

A phase III trial of Arzerra as a maintenance therapy for chronic lymphocytic leukemia met its primary endpoint of extending progression-free survival at an interim analysis.

The study evaluated Arzerra (ofatumumab) maintenance therapy versus no further treatment and observation in patients with relapsed CLL who responded to treatment at relapse.

The independent data monitoring committee did not identify any new safety signals and will continue to monitor patients for safety until all study patients complete therapy.

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Stomach Cancer

TCGA Researchers Discover Stomach Cancer Falls Into Four Distinct Molecular Subtypes

Researchers with The Cancer Genome Atlas Network found that stomach cancers fall into four distinct molecular subtypes.

Previous attempts to examine the clinical characteristics of gastric cancer were hindered by how differently cancer cells can look under a microscope, even when from the same tumor. Researchers say the new classification system can serve as a valuable adjunct to the current pathology classification system, which has two categories: diffuse and intestinal.

The researchers identified the new subgroups through complex statistical analyses of molecular data from 295 tumors. They used six molecular analysis platforms including DNA sequencing, RNA sequencing, and protein arrays. The study was published in Nature.

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FDA News

FDA Approves Avastin Combination For Late-Stage Cervical Cancer

FDA approved a new use for Avastin (bevacizumab) to treat patients with persistent, recurrent or late-stage cervical cancer. The new indication is approved for use in combination with paclitaxel and cisplatin or in combination with paclitaxel and topotecan.

"Avastin is the first drug approved for patients with late-stage cervical cancer since the 2006 approval of topotecan with cisplatin," said Richard Pazdur, director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "It is also the first biologic agent approved for patients with late-stage cervical cancer and was approved in less than four months under the FDA's priority review program."

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Arzerra Maintenance Therapy Extends PFS in Phase III Trial

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Further analysis of the safety and efficacy data is underway and will be shared with regulators and the scientific community in the coming months, according to Arzerra's sponsors, GlaxoSmithKline plc and Genmab A/S.

Patients in the ofatumumab arm of the study, named PROLONG, received an initial dose of 300 mg of ofatumumab, followed one week later by a second dose of 1,000 mg, then doses of 1,000 mg every eight weeks for up to two years, while patients in the observation treatment arm receive no further treatment.

Arzerra is a monoclonal antibody designed to target the CD20 molecule found on the surface of CLL cells and normal B lymphocytes. It is not approved or licensed anywhere in the world as maintenance treatment for relapsed CLL.

In the U.S., ofatumumab is approved for use in combination with chlorambucil for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate.

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Breast Cancer

Phase III Nexavar Trial Fails Primary Endpoint

A phase III trial of Nexavar tablets in patients with advanced breast cancer did not meet its primary endpoint of extending progression-free survival.

The study, called RESILIENCE, evaluated Nexavar (sorafenib) in combination with capecitabine compared to capecitabine plus placebo in patients with HER2-negative breast cancer who are resistant to or have failed prior taxane therapy, and resistant to or failed anthracycline or for whom further anthracycline therapy is not indicated.

Based on initial review of the data, the types of adverse events observed were generally comparable with those known for either sorafenib or capecitabine. Data from this study are expected to be presented at an upcoming scientific congress, according to the drug's sponsors, Bayer HealthCare and Onyx Pharmaceuticals Inc.

RESILIENCE was a randomized, double-blind study that enrolled 537 patients in more than 20 countries.

Secondary endpoints of the trial included overall survival, time to progression, overall response rate, disease control rate, duration of response, patient reported quality of life and safety.

Patients were randomized to receive either 600 mg of oral sorafenib or matching placebo daily on a continuous schedule, in addition to 1,000 mg/m(2) of capecitabine twice daily for 14 days of a 21 day cycle.

Nexavar is approved in the U.S. for the treatment of patients with unresectable hepatocellular carcinoma, patients with advanced renal cell carcinoma and patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma refractory to radioactive iodine treatment.

It is thought to inhibit both the tumor cell and tumor vasculature. In in vitro studies, Nexavar has been shown to inhibit multiple kinases thought to be involved in both cell proliferation and angiogenesis. These kinases include Raf kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-B, KIT, FLT-3 and RET.

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Phase II ThermoDox Trial Demonstrates Positive Response

Interim data from an ongoing open-label phase II trial of ThermoDox in recurrent chest wall breast cancer demonstrated positive local response rates in combination with mild hyperthermia.

The trial, named DIGNITY, is designed to enroll 20 patients at several U.S. clinical sites—of the 13 patients enrolled and treated, 10 were eligible for evaluation of efficacy.

Sixty percent of patients experienced a stabilization of highly refractory disease with a local response rate of 50 percent, notably three complete responses, two partial responses and one patient with stable disease.

These data are consistent with the previously reported positive phase I data in RCWBC.

Celsion Corporation, the drug's sponsor, previously reported combined clinical data from two phase I trials, the phase 1 DIGNITY study and the Duke University-sponsored phase I trial of ThermoDox plus hyperthermia in RCWBC.

"In this population, tumor response is a clinically meaningful endpoint," said Nicholas Borys, Celsion's senior vice president and chief medical officer. "Unchecked, progression of recurrent chest wall lesions results in severe and debilitating complications."

Stomach Cancer

TCGA Researchers Discover Four Stomach Cancer Subtypes

(Continued from page 1)

"A key advance with this project is that we have identified and developed a much more useful classification system to find groups of gastric cancer that have distinct molecular features, and at the same time, we also identified key targets to pursue in different groups of patients," said Adam Bass, of Harvard Medical School and Dana-Farber Cancer Institute, and one of the lead investigators on the project.

Tumors in the first group, which represented 9 percent of the tumors, were positive for Epstein-Barr virus and had several other molecular commonalities.

Tumors in a second subgroup, accounting for 22 percent of the tumors, had high microsatellite instability, which is the tendency for mutations to accumulate in repeated sequences of DNA.

The remaining subgroups differed in the level of somatic copy number alterations, which can result from duplication or deletion of sections of the genome. The tumors in the third subgroup, which comprised 20 percent of the tumors, were considered to have a low level of SCNAs and were called genomically stable. The remaining 50 percent of tumors were classified as chromosomally unstable, with a high level of SCNAs.

The EBV-positive subgroup of tumors was of particular interest. EBV is best known in the U.S. as the cause of infectious mononucleosis, which is characterized by fever, sore throat, and swollen lymph glands, especially in the neck.

EBV is also suspected of causing certain cancers, including nasopharyngeal carcinoma and some types of lymphoma. Previous research had shown that EBV can be detected in a minority of gastric adenocarcinomas and that EBV genes are expressed in those tumors. However, this study found that the presence of EBV in gastric tumors is associated with a number of other molecular characteristics.

First, the researchers observed that EBV-positive tumors displayed a high frequency of mutations in the PIK3CA gene, which codes for a component of a protein, PI3-kinase, which is essential for cell growth and division and many other cellular activities that are important in cancer.

Although 80 percent of EBV-positive tumors harbored a protein-changing alteration in PIK3CA, PIK3CA mutations were found in 3 to 42 percent of tumors of the other gastric cancer subtypes. The scientists suggested that EBV-positive tumors might respond to PI3-kinase inhibitors, some of which are in the early stages of testing in clinical trials but are not yet approved by the FDA for general use.

Some tumors in the EBV-positive subgroup also showed more gene copies being produced in a chromosomal region that contains the JAK2 gene. The JAK2 protein facilitates cell growth and division, and the increased expression of JAK2 may inappropriately activate cell growth. The amplified region also contains the genes for two proteins, PD-L1 and PD-L2, which suppress immune responses; their increased expression may help tumors escape destruction by the immune system. The investigators suggested that these findings support the evaluation of JAK2 inhibitors and PD-L1/2 antagonists for the treatment of EBV-positive gastric cancers.

And the EBV-positive subgroup showed a far higher prevalence of DNA hypermethylation than any other cancer subtype reported by TCGA researchers. In the EBV-positive tumor subgroup, hypermethylation was most often observed in the promoter regions of

genes, which would prevent the expression of the genes.

Important insights also came from analyses of the three other gastric cancer subgroups. For example, tumors of the genomically stable subtype contained frequent mutations in a gene called RHOA, whose product interacts with other cellular proteins to help cells change shape and migrate, which may be important in tumor growth. This finding suggests possible targets for treating tumors of this subtype.

And tumors of the chromosomal unstable subtype contained frequent amplifications of genes that encode receptor proteins on the outside of the cell, leading to the promotion of aberrant cell growth. Drugs are already available to curb the activity of some of these proteins.

Lymphoma

Researchers Find Two Types Of MCL Drug Resistance

Genomic analyses of tissues from mantle cell lymphoma patients helped researchers explain two types of drug resistance and ways to overcome them in the clinic.

In the study—published in Cancer Discovery, a journal of the American Association for Cancer Research—researchers examined mantle cell lymphoma patients that failed to respond to treatment with ibrutinib (Imbruvica), or initially responded, but then stopped and progressed.

"Ibrutinib, a drug that targets a protein called BTK, shows unprecedented clinical activity against mantle cell lymphoma," said Selina Chen-Kiang, professor of pathology and laboratory medicine and professor of microbiology and immunology at Weill Cornell Medical College. "However, the drug doesn't work for about 32 percent of patients, and their lymphomas are said to have primary resistance to ibrutinib. We are also learning that most patients whose lymphomas respond to ibrutinib eventually relapse because their tumors acquire resistance to the drug."

"The knowledge that we gained from longitudinal RNA and genomic sequencing of mantle cell lymphomas with primary and acquired resistance to ibrutinib allowed us to identify rational drug combinations that may overcome resistance in these two settings," continued Chen-Kiang. "We recently opened a clinical trial to test one of these combinations, the selective CDK4/6 inhibitor palbociclib and ibrutinib [NCT02159755]."

Researchers used whole-exome and whole-transcriptome analysis of five serial biopsies from a patient who had mantle cell lymphoma that initially responded to ibrutinib before progressing to identify reasons why mantle cell lymphomas acquire resistance to ibrutinib.

After comparing these data with results from analysis of healthy tissues from the same patient, the researchers found that a mutation in BTK, the C481S mutation, appeared at relapse. The same mutation was detected at relapse in a second patient who had mantle cell lymphoma with acquired resistance to ibrutinib but not in any patients with primary resistance to the drug.

Further analyses revealed the consequences of the relapse-specific BTK C481S mutation, including activation of the PI3K and CDK4 signaling pathways, which promote cell survival and proliferation. Blocking CDK4 with the investigational anticancer drug palbociclib made ibrutinib-resistant lymphoma cells carrying the BTK C481S mutation sensitive to investigational drugs that inhibit PI3K. In addition, palbociclib made ibrutinib-resistant lymphoma cells harboring normal BTK sensitive to both ibrutinib and investigational drugs that inhibit PI3K.

Human Papillomavirus

International Working Group Suggests Earlier Endpoints For HPV Vaccine Trials

A report from an international working group of researchers suggests that the process of evaluating human papillomavirus vaccines can be significantly shortened.

The group, convened by NCI and the International Agency for Research on Cancer, examined evidence to determine whether vaccine efficacy can be established at an earlier stage of virological infection, rather than clinical onset of disease in the cervix. They also looked at whether immunobridging trials could be sufficient for licensure under specific circumstances.

The group concluded that for most situations, such as infection of the cervix or anus of young adults (e.g. individuals aged 16–26 years), "persistent HPV infection of 6 months or longer be used as an appropriate end-point when protection is being evaluated, with reduction in disease being verified by post-licensure monitoring."

"If vulvar/vaginal protection is to be evaluated in a trial, it is recommended to use HPV 16/18-positive high-grade vulvar intraepithelial neoplasia/vaginal intraepithelial neoplasia (VIN/VAIN) as a disease end-point, as there is relatively little experience in using persistent HPV infection as a surrogate end-point for vulvar and vaginal disease," the report continued. "A

persistent infection end-point could be considered at these two sites if subsequent studies validated the ability to detect persistent infection at these sites."

The report, titled Primary End-points for Prophylactic HPV Vaccine Trials, provides a series of technical recommendations for clinical efficacy trials.

"These recommendations could help reduce the cost and duration of clinical studies and facilitate research in important areas, such as reducing the number of doses of the current vaccine, or evaluating new vaccines similar to those already licensed," said Rolando Herrero, head of the Prevention and Implementation Group at IARC and organizer of the working group.

Multiple Myeloma

Phase III Kyprolis Trial Fails OS Primary Endpoint

The phase III FOCUS clinical trial of Kyprolis in multiple myeloma did not meet its primary endpoint of improving overall survival.

The 315-patient, open-label study evaluated Kyprolis (carfilzomib) for Injection compared to an active control regimen of low-dose dexamethasone, or equivalent corticosteroids, plus optional cyclophosphamide in patients with relapsed and advanced refractory multiple myeloma.

Nearly all patients in the control arm received cyclophosphamide. Patients were heavily pretreated and had received a median of five therapeutic regimens prior to study entry. Detailed results will be submitted for presentation at an upcoming scientific meeting.

Secondary trial endpoints included progression-free survival, overall response rate, clinical benefit rate, duration of response and safety.

Patients were randomized to receive Kyprolis (20mg/m(2) on days 1 and 2 of cycle 1 followed by 27mg/m(2) on days 8, 9, 15, and 16 of cycle 1 and all doses cycle 2 through 9, and 27 mg/m(2) on days 1,2,15, and 16 of cycle 10 and beyond) or an active control regimen of oral steroids and optional cyclophosphamide.

Treatment discontinuation due to adverse events and on-study deaths were comparable between the two arms. There was an increase in the incidence of renal adverse events of all grades observed in the Kyprolis arm compared to the active control arm and the label. The rate of cardiac events observed in the Kyprolis arm was consistent with the current U.S. Kyprolis label.

In July 2012, FDA granted accelerated approval to Kyprolis for Injection for multiple myeloma patients who have received at least two prior therapies including bortezomib and an immunomodulatory agent, and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval was based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

Kyprolis is marketed in the U.S. by Onyx Pharmaceuticals, an Amgen subsidiary.

Kidney Cancer

Researchers Plan to Extend Phase IIa Asonep Trial

Based on progression-free survival data, a single-arm, open-label phase IIa study of Asonep in metastatic renal cell carcinoma will be extended to a second cohort.

The decision followed an interim analysis of RCC patients that have failed at least one therapy involving a VEGF inhibitor and no more than one mTOR inhibitor, with a maximum of three failed treatments in all. This patient population is considered "last line," and the literature suggests cancer progression in this population within a one-to-two month time frame, according to Asonep's sponsor, Lpath Inc.

Lpath has enrolled 26 patients in the study. Asonep has a favorable safety profile thus far, with no drug-related serious adverse events.

The first 17 patients were initiated at a dose of 15 mg/kg. Of these, seven had progressive disease at or before the end of four months; eight were progression-free at the four-month mark—with one of these patients deemed a partial responder, and three experiencing reduced tumor volume, but not enough to be categorized as a partial responder. Two exited the study due to serious adverse events unrelated to the drug prior to the four-month mark, and are not considered evaluable.

Notably, of the eight patients that were stable or better as of the fourth month, two are now in month 15 of the study, one is in month 13, and one is in month 10. An additional patient was stable through month seven, but then missed six treatments during a vacation, and shortly thereafter progressed.

The next nine patients were initiated at a dose of 24 mg/kg. Of these higher-dose patients: four had progressive disease at or before the end of four months; two were progression-free at the four-month mark (with one deemed a partial responder); and the remaining three have not yet reached their four-month mark.

"A bimodal distribution of patients has emerged, whereby half the patients experience disease progression early, consistent with their 'last line' prognosis, while the other half experience stable disease, with a number

of them still progression-free beyond one year," said Dario Paggiarino, Lpath chief development officer. "Based on the safety profile and the promising results, we have moved beyond the first cohort of 22 evaluable patients into a second cohort, allowing us to enroll up to a total of 54 evaluable patients."

Lpath says it will consider studying Asonep in RCC patients as a first-line or second-line treatment in combination with other drugs, as well as in patients with other tumor types, either in combination or as a single agent. This trial has been partially funded by a $3 million grant from NCI under its Small Business Innovation Research Program.

Smoking and Survivorship

Study: Nine Years After Diagnosis 9.3% of Survivors Still Smoke

Nine years after diagnosis, 9.3 percent of U.S. cancer survivors were current smokers and 83 percent of these individuals were daily smokers who averaged 14.7 cigarettes per day, according to a study performed by researchers at the American Cancer Society.

"We need to follow up with cancer survivors long after their diagnoses to see whether they are still smoking and offer appropriate counseling, interventions, and possible medications to help them quit," said Lee Westmaas, director of tobacco research at ACS and lead author of the study.

The report was published in Cancer Epidemiology, Biomarkers & Prevention, a journal of the American Association for Cancer Research.

Researchers analyzed data on 2,938 patients nine years after their diagnoses. Survivors were more likely to smoke if they were younger, had less education and income, or drank more alcohol. About 40 percent of smokers said they planned to quit within the next month, but this intention was lower among survivors who were married, older, or smoked more.

By cancer type, smoking prevalence among patients was: 17.2 percent in bladder cancer; 14.9 percent in lung cancer; 11.6 percent in ovarian cancer; 7.6 percent in melanoma; 7.3 percent in kidney cancer; and 6.8 percent in colorectal cancer.

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NCI CTEP-Approved Trials For the Month of August

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

9571: A Phase IB Study of the Combination of AZD6244 Hydrogen Sulfate (Selumetinib) and Cyclosporin A (CsA) in Patients with Advanced Solid Tumors with an Expansion Cohort in Metastatic Colorectal Cancer. University of Texas MD Anderson Cancer Center; LAO Lieu, Christopher Hanyoung. (303) 724-6390

Phase I/II

9577: Phase 1 Study of Ibrutinib and Immuno-Chemotherapy Using Dose-Adjusted-Temozolomide, Etoposide, Doxil, Dexamethasone, Ibrutinib, Rituximab (DA-TEDDI-R) in Primary CNS Lymphoma. NCI Lymphoid Malignancies Branch; Dunleavy, Kieron Michael. (301) 435-1007

Phase II

9568: A Randomized Placebo-Controlled Phase II Trial Comparing Gemcitabine Monotherapy to Gemcitabine in Combination with AZD 1775 (MK 1775) in Women with Recurrent, Platinum Resistant Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers. University Health Network-Princess Margaret Hospital; Oza, Amit M. (416) 946-2818

NRG-LU001: Randomized Phase II Trial of Concurrent Chemoradiotherapy Metformin HCL in Locally Advanced NSCLC. NRG Oncology; Tsakiridis, Theodoros. (905) 387-9495

S1314: A Randomized Phase II Study of CO-eXpression ExtrapolatioN (COXEN) with Neoadjuvant Chemotherapy for Localized, Muscle-Invasive Bladder Cancer. SWOG; Flaig, Thomas W. (303) 724-3888

S1406: Randomized Phase II Study of Irinotecan and Cetuximab with or Without Vemurafenib in BRAF Mutant Metastatic Colorectal Cancer. SWOG; Kopetz, Edmund Scott. (713) 792-2828

Phase III

ANBL1232: Utilizing Response- and Biology-Based Risk Factors to Guide Therapy in Patients with

Non-High-Risk Neuroblastoma. Children's Oncology Group; Meany, Holly J. (202) 476-2800

E4512: A Phase III Double-Blind Trial for Surgically Resected Early Stage Non-Small Cell Lung Cancer: Crizotinib Versus Placebo for Patients with Tumors Harboring the Anaplastic Lymphoma Kinase (ALK) Fusion Protein. ECOG-ACRIN Cancer Research Group; Gerber, David Eric. (214) 648-4180

S1316: Prospective Comparative Effectiveness Trial for malignant Bowel Obstruction. SWOG; Krouse, Robert Scott. (520) 626-4703

Pilot Phase

9622: A Pilot Study of 18F-DCFBC PET/CT in Prostate Cancer. National Cancer Institute Molecular Imaging Program; Lindenberg, Maria Liza. (301) 443-0604

Other Phases

A151216: Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST). Alliance for Clinical Trials in Oncology; Janne, Pasi Antero. (617) 632-6076

AALL13B5-Q: Development and Implementation of a Novel Prognostic Test in ALL. Children's Oncology Group; Miles, Rodney R. (801) 213-3448

ACNS14B1-Q: STAT3 Signaling in Medulloblastoma. Children's Oncology Group; Lin, Jiayuh. (614) 722-5086

AEWS13B3-Q: Investigating G-Protein Coupled Receptors (GPCRs) as Biomarkers of Aggressive Disease and Novel Therapeutic Targets in Ewing Sarcoma. Children's Oncology Group; Lawlor, Elizabeth Rachel. (734) 615-4814

ANBL14B2-Q: The Role of CIP75 as an Oncogene in Childhood Neuroblastoma. Children's Oncology Group; Barlos, Vivian. (808) 956-2712

ANBL14B3-Q: Prevalence and Clinical Correlations of Somatostatin Receptor-2 (SSTR2) Expression in Neuroblastoma. Children's Oncology Group; Baruchel, Sylvain. (416) 813-7795

E2993T6: Role of Ikaros in the Biology and Therapy of High-Risk Precursor B-Cell Leukemia. ECOG-ACRIN Cancer Research Group; Van Etten, Richard A. (949) 824-2655

EA914LT2: Genetic Analyses of Relapsed ALL. ECOG-ACRIN Cancer Research Group; Ferrando, Adolfo A. (212) 851-4611

FDA News

Avastin Combination Approved For Late-Stage Cervical Cancer

(Continued from page 1)

Avastin interferes with the blood vessels that fuel the development of cancerous cells. Avastin is also approved in the U.S. to treat cancers of the colon, kidney, and lung. The approval in advanced cervical cancer was based on the GOG-0240 study, which enrolled 452 participants with persistent, recurrent, or late-stage disease.

Participants were randomly assigned to receive paclitaxel and cisplatin with or without Avastin or paclitaxel and topotecan with or without Avastin. Results showed an increase in overall survival to 16.8 months in participants who received chemotherapy in combination with Avastin as compared to 12.9 months for those receiving chemotherapy alone.

GOG-0240 is an independent, NCI-sponsored study of the Gynecologic Oncology Group. Avastin is marketed by Genentech, a member of the Roche Group.

FDA approved Cologuard, the first stool-based colorectal screening test that detects the presence of red blood cells and DNA mutations that may indicate the presence of certain kinds of abnormal growths that may be cancers such as colon cancer or precursors to cancer.

Using a stool sample, Cologuard detects hemoglobin and certain mutations associated with colorectal cancer in the DNA of cells shed by advanced adenomas as stool moves through the large intestine and rectum. Patients with positive test results are advised to undergo a diagnostic colonoscopy.

The Centers for Disease Control and Prevention estimate that if everyone age 50 or older had regular

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screening tests as recommended, at least 60 percent of colorectal cancer deaths could be avoided.

"This approval offers patients and physicians another option to screen for colorectal cancer," said Alberto Gutierrez, director of the Office of In Vitro Diagnostics and Radiological Health at the FDA's Center for Devices and Radiological Health. "Fecal blood testing is a well-established screening tool and the clinical data showed that the test detected more cancers than a commonly used fecal occult test."

This approval does not change current practice guidelines for colorectal cancer screening. Stool DNA testing is not currently recommended as a method to screen for colorectal cancer by the U.S. Preventive Services Task Force. Among other guidelines, the USPSTF recommends adults age 50 to 75, at average risk for colon cancer, be screened using fecal occult blood testing, sigmoidoscopy or colonoscopy.

The safety and effectiveness of Cologuard was established in a clinical trial that screened 10,023 subjects. The trial compared the performance of Cologuard to the fecal immunochemical test, a non-invasive screening test that detects blood in the stool.

Cologuard accurately detected cancers and advanced adenomas more often than FIT, detecting 92 percent of colorectal cancers and 42 percent of advanced adenomas in the study population, while FIT screening detected 74 percent of cancers and 24 percent of advanced adenomas.

Cologuard was less accurate than FIT at correctly identifying subjects negative for colorectal cancer or advanced adenomas. Cologuard correctly gave a negative screening result for 87 percent of the study subjects, while FIT provided accurate negative screening results for 95 percent of the study population, according to Cologuard's sponsor, Exact Sciences.

The Centers for Medicare & Medicaid Services issued a proposed national coverage determination for Cologuard. Cologuard is the first product reviewed through a joint FDA-CMS pilot program known as parallel review where the agencies concurrently review medical devices to help reduce the time between the FDA's approval of a device and Medicare coverage.

This voluntary pilot program is open to certain premarket approval applications for devices with new technologies and to medical devices that fall within the scope of a Part A or Part B Medicare benefit category and have not been subject to a national coverage determination.

"Parallel review allows the last part of the FDA process to run at the same time as the CMS process, cutting as many as six months from the time from study initiation to coverage," said Nancy Stade, CDRH's deputy director for policy. "The pilot program is ongoing, but we will apply what we have learned to improve the efficiency of the medical device approval pathway for devices that address an important public health need."

"This is the first time in history that FDA has approved a technology and CMS has proposed national coverage on the same day," said Patrick Conway, chief medical officer and deputy administrator for innovation and quality for CMS. "This parallel review represents unprecedented collaboration between the two agencies and industry and most importantly will provide timely access for Medicare beneficiaries to an innovative screening test to help in the early detection of colorectal cancer."

CMS proposes to cover the Cologuard test once every three years for Medicare beneficiaries who meet all of the following criteria: age 50 to 85 years; asymptomatic, including but not limited to lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test; and an average risk of developing colorectal cancer, including no personal history of adenomatous polyps, of colorectal cancer, or inflammatory bowel disease, including Crohn's Disease and ulcerative colitis.

Health Canada approved Abraxane for Injectable Suspension for first-line treatment of adult patients with metastatic pancreatic cancer, representing the first approved treatment for this disease in nearly two decades.

Approval of Abraxane (paclitaxel powder for injectable suspension; nanoparticle, albumin-bound paclitaxel) was based on the results of MPACT, an open-label, phase III, randomized, international study which was published in the New England Journal of Medicine in October 2013.

The study involved 861 chemotherapy-naïve patients with metastatic pancreatic cancer from 11 countries, including Canada, and showed a statistically significant improvement in median overall survival with Abraxane plus gemcitabine compared to gemcitabine alone: 8.5 vs. 6.7 months, respectively (HR 0.72, P<0.0001); a 28 percent overall reduction in risk of death.

"It's been quite some time since we've seen any type of treatment advance for pancreatic cancer making this news so important for patients." said Laurie Ellies, co-founder and acting executive director of Pancreatic Cancer Canada. "Over the past decade, there has been

a significant improvement in cancer survival rates. Sadly, the same cannot be said about pancreatic cancer.

"This year alone, we can expect an estimated 4,700 Canadians will be diagnosed with this disease."

Abraxane is formulated with albumin, a human protein, and is free of solvents. Abraxane in combination with gemcitabine for the treatment of metastatic pancreatic cancer is approved in the U.S. and 30 other countries.

The European Medicines Agency approved Eisai's request for accelerated assessment of lenvatinib for the treatment of patients with progressive radioiodine-refractory differentiated thyroid cancer.

Lenvatinib is an oral multiple receptor tyrosine kinase inhibitor with a novel binding mode that selectively inhibits the kinase activities of vascular endothelial growth factor receptors, in addition to other proangiogenic and oncogenic pathway-related RTKs, including fibroblast growth factor receptors, the platelet-derived growth factor receptor PDGFRalpha, KIT, and RET.

Lenvatinib received orphan drug designation for the treatment of follicular and papillary thyroid cancer from the European Commission in April 2013.

The EU marketing authorization application will be based on the results of the Phase III SELECT trial of lenvatinib that demonstrated extended progression free survival compared to placebo (HR=0.21, [99% CI, 0.14-0.31]; p<0.0001). The median lengths of PFS of lenvatinib and placebo were 18.3 and 3.6 months, respectively.

Secondary endpoints of the study included overall response rate, overall survival and safety. The study enrolled 392 patients in over 100 sites in Europe, North and South America and Asia and was conducted by Eisai in collaboration with the SFJ Pharmaceuticals Group. Eisai expects to file for lenvatinib in the next few months.

Sanofi US launched an authorized generic version of Eloxatin (oxaliplatin injection) through Winthrop US, the company's generics division. Sanofi's authorized generic version is the same formulation as the original drug, for which the company holds the original patent.

Eloxatin is a platinum-based drug used in combination with infusional 5-fluorouracil/leucovorin. This treatment is indicated for treatment of advanced colorectal cancer or as adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor. The authorized generic version of Eloxatin will be available in the same sizes: 50 mg and 100 mg single-use vials.

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