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THE
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Cancer research news for clinicians

Melanoma

Yervoy-Nivolumab Combination Treatment Shrinks Tumors 80 Percent in Three Months

Combination therapy with Yervoy (ipilimumab) and the investigational antibody drug nivolumab led to lasting tumor shrinkage in approximately half of patients with aggressive, advanced melanoma—much better than either treatment individually—in a phase I study presented at the annual meeting of the American Society of Clinical Oncology.

Within the first three months of treatment, three out of four patients who responded to the combination treatment experienced tumor reduction—with 31 percent of patients having their tumors shrink by more than 80 percent.

Patients with inoperable stage III and IV metastatic melanoma who had undergone up to three prior therapies were assigned to six different treatment arms. The current results are based on 52 patients in three completed treatment arms, in which patients received concurrent treatment with the two drugs.

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Colorectal Cancer

Single-Agent Phase III Trial Comparing Vectibix to Erbitux Meets Primary Endpoint

A phase III study comparing Vectibix to Erbitux as a single agent for the treatment of chemorefractory metastatic colorectal cancer in patients with wild-type KRAS tumors met its primary endpoint of non-inferiority for overall survival.

The estimated overall survival hazard ratio was 0.966 (95% CI: 0.839, 1.113) favoring the Vectibix (panitumumab) arm. Overall, the relative adverse event profiles were as anticipated for each of the anti-EGFR therapies studied, including known events such as rash, diarrhea and hypomagnesemia.

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Non-Small Cell Lung Cancer

Trial Shows Standard-Dose Radiotherapy Safer, More Effective than Higher Doses

A phase III trial in patients with stage III non-small cell lung cancer demonstrated that standard dose radiotherapy is safer and more effective than high-dose radiotherapy, extending survival by nine months and causing fewer treatment related deaths.

While 60 Gy is already standard, many doctors use higher doses, such as 74 Gy, expecting better outcomes. In the study, 464 patients were randomly assigned to treatment with standard- or high-dose radiation therapy along with standard chemotherapy with paclitaxel and carboplatin.

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Yervoy-Nivolumab Combination Leads to Tumor Shrinkage

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In those three arms, tumor shrinkage rates were 21, 53, and 50 percent, with the highest rates seen in patients treated with the highest dose of both drugs.

Nivolumab and Yervoy, both developed by Bristol-Meyers Squibb, are antibody drugs that interfere with immune system checkpoints that normally inhibit the immune system's ability to attack cancer cells. Yervoy targets CTLA-4 and has prolonged survival in phase III trials, while nivolumab targets PD-1. PD-1 is induced by the blocking of CTLA-4, and targeting both together has shown enhanced antitumor activity.

Two of the remaining three arms enrolled patients who had undergone prior Yervoy treatment, and received only nivolumab on this study. Those data are still preliminary, but it appears that patients who initially had little benefit from Yervoy had significant tumor shrinkage after subsequent treatment with nivolumab.

"Melanoma researchers have been hopeful that combination regimens would increase the effectiveness of single-agent immunotherapies, and now we have confirmation that such an approach has significant potential," said Jedd Wolchok, a medical oncologist at Memorial Sloan-Kettering Cancer Center. "The complete and near-complete response rates we're seeing are unprecedented for an immunotherapy in melanoma."

A randomized phase III trial of the nivolumab/Yervoy combination as first-line therapy for patients with advanced melanoma is scheduled to begin in June.

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Glioblastoma Multiforme

Vaccine Increases PFS 146%, OS 60% In Phase II Clinical Trial

A phase II clinical trial showed that newly diagnosed glioblastoma multiforme patients treated with the Prophage G-100 vaccine plus the standard of care showed a 146 percent increase in progression free survival and a 60 percent increase in overall survival compared to the standard of care.

The single-arm trial of the vaccine, Heat Shock Protein-Peptide Complex-96, enrolled 46 patients at eight centers across the U.S.

Patients were treated with radiation and temozolomide as the standard of care in addition to receiving HSPPC-96 vaccination. Results were presented at the annual scientific meeting of the American Association of Neurological Surgeons.

Analyses of data show a median PFS of 17 months; compared to the reported PFS of radiation treatment and temozolomide alone, which is 6.9 months. Median OS in patients treated with HSPPC-96 was 23.3 months, compared to the standard of care OS of 14.6 months. The majority of enrolled patients in the trial are still being followed and it is expected that PFS and OS will continue to mature as more data are collected, according to the vaccine's sponsor, Agenus Inc.

Thirty-two patients enrolled and treated at University of California, San Francisco, also underwent testing for expression of B7-H1 in blood samples taken prior to surgery. Glioblastoma has been shown to induce systemic immunosuppression through stimulation of B7-H1 expression, which could affect the efficacy of immunotherapy.

These exploratory analyses showed that patients with low expression of B7-H1 (53 percent) had better PFS (21.6 months) than those with high B7-H1 (47 percent) expression (11.4 months).

NCI's Cancer Therapy Evaluation Program is supporting a study of the HSPPC-96 vaccine in a large, randomized phase II trial in combination with Avastin (bevacizumab) in patients with surgically resectable recurrent GBM. That study is being sponsored by the Alliance for Clinical Trials in Oncology.

The Alliance trial will investigate the benefits of treatment with a combination of HSPPC-96 and Avastin in a three-arm study of 222 patients with surgically resectable recurrent GBM using a primary endpoint of overall survival.

The study will compare efficacy of the HSPPC-96

vaccine administered with bevacizumab either concomitantly or at progression, versus treatment with bevacizumab alone.

In addition to the newly diagnosed GBM study with G-100 and the Alliance trial, a phase II study testing the Prophage Series G-200 in patients with recurrent glioma is underway. Agenus expects the final trial results of this study to be published in a scientific journal in 2013.

Sarcoma

Cediranib Demonstates Control In Alveolar Soft Part Sarcoma

Patients with advanced alveolar soft part sarcoma achieved some control of their disease using the experimental drug cediranib in a phase II trial.

ASPS accounts for less than 1 percent of soft tissue sarcomas and occurs mostly in people ages 15 to 35. The median survival time for patients with unresectable metastatic ASPS is 40 months, with a 5-year survival rate of 20 percent.

Cediranib inhibits vascular endothelial growth factor receptors which regulate blood vessel formation, and has been tested in clinical trials against other cancers, including non-small cell lung cancer, kidney cancer, and colorectal cancer, with varying degrees of benefit.

The 43 enrolled patients with metastatic ASPS were given a 30 milligram oral dose of cediranib once daily until either their disease progressed or they developed significant side effects. The objective response rate, which requires a more than 30 percent reduction in tumor size of target lesions, is 35 percent—15 of the 43 patients achieved a partial response. An additional 26 patients, or 60 percent, have stable disease.

Researchers obtained tumor biopsy specimens before treatment and again during the first week of treatment. When comparing gene expression in these two specimen groups, they discovered that samples taken after treatment had lower expression of two genes that are important in regulating blood vessel development: ANGPT2 and FLT1. The results of the trial, the largest to date on ASPS, were published in the Journal of Clinical Oncology.

Researchers have initiated a follow-up trial that is comparing the effectiveness of cediranib to another vascular endothelial growth factor receptor drug, sunitinib, in patients with metastatic ASPS.

Cediranib is developed by AstraZeneca.

Colorectal Cancer

Vectibix-Erbitux Trial Meets Overall Survival Endpoint

(Continued from page 1)

The international, open-label trial, ASPECCT, enrolled 1,010 patients with wild-type KRAS tumors and randomized them to receive either Vectibix or Erbitux (cetuximab). Secondary endpoints included safety, patient reported outcomes, progression-free survival, time to response, time to treatment failure and duration of response.

Vectibix is the first fully human anti-epidermal growth factor receptor antibody approved by FDA for the treatment of metastatic colorectal cancer. Vectibix was approved in the U.S. in September 2006 as a single agent for the treatment of metastatic colorectal carcinoma with disease progression on or following fluoropyrimidine, oxaliplatin and irinotecan chemotherapy regimens.

Vectibix is not indicated for the treatment of patients with KRAS mutation-positive mCRC or for whom KRAS mCRC status is unknown. Retrospective subset analyses of mCRC trials have not shown a treatment benefit for Vectibix in patients whose tumors had KRAS mutations in codon 12 or 13.

Detailed safety and efficacy data will be submitted at an upcoming meeting later this year, according to Amgen, Vectibix's sponsor. In Europe, the trial is a Specific Obligation for Vectibix as part of the European Medicine Agency's conditional marketing authorization.

Immunotherapy

Antibody Targeting PD-L1 Shows Fast Tumor Shrinkage

A phase I expansion study of MPDL3280A showed tumor shrinkage rates in patients with several different cancers, including lung, kidney, colorectal and gastric cancers and melanoma, which had progressed after several treatments.

The drug, an engineered PD-L1 targeted antibody, was safe and produced durable responses, with nearly all responses still ongoing. Several patients experienced tumor shrinkage within days of starting treatment. Importantly, many patients reported improvement in their cancer-related symptoms, such as no longer requiring oxygen supplementation or decreased need for narcotics to control pain.

The study was presented at the annual meeting of the American Society of Clinical Oncology.

PD-L1 is frequently overexpressed on the surface

of cancer cells, allowing them to hide from the immune system. When MPDL3280A attaches to the PD-L1 protein, it allows the body's T-cells to fight the cancer.

Efficacy was evaluated in 140 patients with locally advanced or metastatic solid tumors whose disease had progressed despite prior therapies. Tumor shrinkage was observed in patients with non-small cell lung cancer, melanoma, renal cell carcinoma, colorectal cancer, and gastric cancer.

Overall, 29 out of 140 (21 percent) patients experienced significant tumor shrinkage and the highest number of therapy responses occurred in patients with lung cancer and melanoma. Therapy responses are still ongoing, with 26 out of 29 responders continuing to respond.

It is not yet clear how PD-L1 expression affects response to MPDL3280A. Using an investigational diagnostic test, researchers analyzed archived tumor tissue from 103 patients and found that tumor shrinkage occurred in 36 percent of patients with PD-L1 positive tumors and, surprisingly, also in 13 percent of patients with PD-L1 negative tumors.

This study has been expanded to include a larger range of solid tumors and blood cancers, with more than 275 patients currently enrolled.

A number of phase II and phase III studies are already planned to confirm the drug's anti-cancer activity and further validate the utility of the PD-L1 diagnostic test. MPDL3280A is sponsored by Genentech Inc.

Non-Small Cell Lung Cancer

Study: Standard-Dose Radiation More Effective than Higher Doses

(Continued from page 1)

In each treatment arm, the patients were also randomly assigned to receive Erbitux (cetuximab) or no additional therapy. Data on the effects of Erbitux on survival will be reported at a later date. The high-dose arm was closed after an interim analysis showed it was not superior to the standard-dose arm.

The median survival for patients who received standard-dose radiation therapy was much longer compared to that in patients who received high-dose radiation therapy—28.7 months compared to 19.5 months—and the estimated 18-month overall survival rates were also higher for the standard-dose arm, at 66.9 percent compared to 53.9 percent.

Cancer recurrence rates at 18 months were higher in the high-dose group of patients. Local recurrence rates were 34.3 vs. 25.1 percent, and distant recurrence rates were 44 vs. 35.3 percent. While the primary cause of death for most patients was lung cancer, there were a notably higher number of treatment-related deaths in the high-dose arm (10), compared to the standard-dose arm (2).

The study was presented at the 2013 annual meeting of the American Society of Clinical Oncology.

Guidelines

Shared Decisionmaking Called For In PSA Screening For Ages 55-69

The American Urological Association released a clinical practice guideline for prostate cancer screening, updating the association's best practice statement on prostate-specific antigen and suggests that the greatest benefit to PSA screening appears to be in men 55 to 69 years old.

The association also published a joint guideline with the American Society for Radiation Oncology on radiation therapy after prostatectomy for patients with and without evidence of prostate cancer recurrence.

The PSA guideline was announced during the association's annual meeting in San Diego. It does not address detection of prostate cancer in symptomatic men. The association recommends that men aged 55 to 69 talk with their physician about the benefits and harms of testing and engage in shared decision-making. The guideline recommends screening every two years instead of annually.

The guideline states that PSA screening in men under 40 is not recommended, nor is routine screening in men at average risk who are between the ages of 40 to 54 years. It also recommends against routine PSA screening in men over 70, or any man with less than a 10-15 year life expectancy.

The ASTRO-AUA guideline recommends that physicians offer adjuvant radiation therapy to patients with adverse pathologic findings at the time of prostatectomy because of demonstrated reductions in recurrence and progression.

The guideline also recommends that clinicians define biochemical recurrence as a detectable or rising PSA value after surgery that is ≥ 0.2 ng/ml, with a second confirmatory level of ≥ 0.2 ng/ml; and that clinicians should consider restaging an evaluation in a patient with a PSA recurrence.

The PSA guideline is available on the AUA website, and a PDF of the AUA-ASTRO guideline can be downloaded from the International Journal of Radiation Oncology • Biology • Physics.

ACCP Publishes Guidelines Recommending Low-Dose CT

The American College of Chest Physicians published new guidelines recommending offering low-dose CT scanning for lung cancer screening to people with significant risk of lung cancer due to age and smoking history.

The guideline showed evidence demonstrating that a structured and specific protocol of lung cancer screening can reduce lung cancer deaths among individuals at an elevated risk of developing lung cancer.

This is a clear change from the prior edition of the guidelines released in 2007, according to the organization. The new guidelines were published as a supplement to CHEST, ACCP's journal.

The guidelines call for the establishment of a registry designed to help address the large number of unanswered questions that arise as screening is implemented, as well as to clarify frequent misconceptions around lung cancer screening among patients and physicians. Additionally, the guidelines call for establishment of quality metrics.

The guidelines also cite research showing that the early inclusion of a palliative care team in the management of advanced lung cancer has meaningful quality of life benefits.

Lymphoma

Study: Routine CT Not Needed In Detecting DLBCL Remissions

The vast majority of diffuse large B cell lymphoma relapses are detected based on symptoms, abnormal blood tests or abnormal findings on physical exam—suggesting that CT scans, which are currently a routine part of follow-up, may be unnecessary, according to a large study.

Researchers found that just 1.5 percent of patients in remission had a relapse that was detected solely through a scheduled imaging scan.

Current surveillance guidelines for DLBCL recommend CT scans no more than every six months for two years after the completion of treatment, and as clinically indicated thereafter. Generally, patients also receive physical exams and blood tests during follow-up.

Researchers assessed post-treatment outcomes in 644 patients enrolled in a prospective, multi-institutional cohort of patients with newly diagnosed DLBCL. All patients had received initial treatment with standard anthracycline based immune-chemotherapy.

During a median follow-up period of 59 months, 109 out of 537 patients (20 percent) who entered post-treatment follow-up experienced a relapse. Overall, at the time of relapse, 68 percent of patients had symptoms, 42 percent had an abnormal finding on physical exam, and 55 percent had abnormalities in blood tests.

Planned surveillance scans detected relapses in only 8 out of 537 of patients before clinical signs appeared.

Some signs of a possible relapse in DLBCL include enlarged lymph nodes, night sweats, unexplained fever, and unintentional weight loss. The study was presented at the annual meeting of the American Society of Clinical Oncology.

Testicular Cancer

Surveillance Following Surgery Sufficient in Stage I Seminoma

A long-term study of men with stage I seminoma, a common form of testicular cancer, suggests that surveillance for cancer recurrence, rather than additional chemotherapy or radiation therapy, is sufficient for the vast majority of men who have undergone successful surgery for their cancer.

Researchers found that 99.6 percent of patients who underwent surveillance only were alive 10 years after their initial diagnosis. Surveillance entails five years of scheduled physical exams, chest X-ray exams, CT scans and blood tests.

Using a nationwide clinical database in Denmark, researchers identified 1,822 patients with stage I seminoma followed on a five year surveillance program. By linking the patient files with national registries they were able to follow the patients for a median period of 15.4 years. All patients had initial surgery to treat their primary cancer.

Overall, 355 of 1,822 patients (19.5 percent) experienced a relapse, which was treated with radiotherapy (216 patients), chemotherapy (136 patients) or surgery (3 patients).

The 10-year cancer-specific survival was 99.6 percent. This rate means that for every 1,000 men followed on a surveillance program, only four die within 10 years.

Researchers found that tumor size larger than 1.5 inches, a spread of disease to blood or lymphatic vessels, and elevated levels of human chorionic gonadotropin increased the risk of relapse. These factors had been associated with high-risk patients in prior, smaller studies. The study was presented at the annual meeting of the American Society of Clinical Oncology.

Cancer Risk

Fitness Reduces Risk of Death From Lung, Colorectal, Prostate Cancer in Middle-Aged Men

A high level of cardiovascular fitness in middle age can reduce the risk of developing and dying from lung or colorectal cancer among men, according to a 20-year study. It also reduces the risk of death from prostate cancer, but not the risk of developing the disease.

The study included 17,049 men who had a single cardiovascular fitness assessment as part of a specialized preventive health check-up visit at a mean age of 50 years offered at the Cooper Institute. The fitness test, which is similar to a stress test for heart disease risk, involved walking on treadmill under a regimen of changing speed and elevation.

Their performance was recorded in metabolic equivalents. Participants were divided into five groups according to their fitness performance.

Researchers subsequently analyzed Medicare claims data to identify the participants of this study who had developed lung, colorectal, or prostate cancer.

Over a median follow-up period of 20-25 years, 2,332 men were diagnosed with prostate cancer, 276 were diagnosed with colorectal cancer, and 277 were diagnosed with lung cancer. There were 347 deaths due to cancer and 159 men died of cardiovascular disease.

Researchers found that the risk of being diagnosed with lung or colorectal cancer was reduced by 68 and 38 percent, respectively, in men who were the most fit, compared to those who were the least fit. Data were adjusted for factors such as smoking, body mass index and age.

Among the men who developed cancer, those who were more fit at middle age had a lower risk of dying from all the three cancers studied, as well as cardiovascular disease.

Even a small improvement in fitness made a significant difference in survival—by reducing the risks of dying from cancer and cardiovascular disease by 14 and 23 percent, respectively.

The study found that men who had low fitness had an increased risk of cancer and cardiovascular disease even if they were not obese. The study was presented at the annual meeting of the American Society of Clinical Oncology.

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NCI CTEP Approved Trials For the Month of May

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

9196: A Phase Ib Trial of Concurrent Cetuximab (Erbitux) and Intensity Modulated Radiotherapy with Ipilimumab (Yervoy) in Locally Advanced Head and Neck Cancer. University of Pittsburgh; Ferris, Robert Louis. (412) 623-1416

9254: A Dose Escalation Study of Ibrutinib with Lenalidomide for Relapsed and Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. University of Colorado Cancer Center - Anschutz Cancer Pavilion; Pollyea, Daniel A. (720) 848-8084

9287: Phase I Dose Escalation of the MET Inhibitor XL184 and the BRAF Inhibitor Vemurafenib. Dana-Farber Cancer Institute; Luke, Jason John. (617) 632-6588

ABTC-1202: Phase I Study of MK-1775 with Radiation and Temozolomide in Patients with Newly Diagnosed Glioblastoma and Evaluation of Intratumoral Drug Distribution in Patients with Recurrent Glioblastoma. Adult Brain Tumor Consortium; Alexander, Brian. (617) 732-6313 X 3

Phase II

9322: A Phase 2 Study of XL184 (Cabozantinib) in Recurrent or Metastatic Endometrial Cancer. University Health Network-Princess Margaret Hospital; Oza, Amit M. (416) 946-2818

9434: Randomized Phase II Study of Intravenous 3-Aminopyridine-2-Carboxaldehyde Thiosemicarbazone (3-AP, Triapine NSC #663249) Cisplatin-Radiochemotherapy Versus Intravenous Cisplatin-Radiochemotherapy in Women Diagnosed with Stage IB-IVA Cervical Cancer and Stage II-IVA Vaginal Cancer. Case Western Reserve University; Kunos, Charles Andrew. (216) 844-3103

A021202: Prospective Randomized Phase II Trial of Pazopanib (NSC #737754, IND 75648) Versus

Placebo in Patients with Progressive Carcinoid Tumors. Cancer and Leukemia Group B; Bergsland, Emily K. (415) 353-7065

A031203: Randomized Phase II Study Comparing Cabozantinib (NSC #761968 and IND #116059) with Commercially Supplied Sunitinib in Patients with Previously Untreated Locally Advanced or Metastatic Renal Cell Carcinoma. Cancer and Leukemia Group B; Choueiri, Toni K. (617) 632-5456

A091201: Randomized Phase II Study Comparing the MET Inhibitor Cabozantinib to Temozolomide/ Dacarbazine in Ocular Melanoma. Cancer and Leukemia Group B; Luke, Jason John. (617) 632-6588

E3311: Phase II Randomized Trial of Transoral Surgical Resection Followed by Low-Dose or Standard-Dose IMRT in Resectable p16+ Locally Advanced Oropharynx Cancer. Eastern Cooperative Oncology Group; Ferris, Robert Louis. (412) 623-0327

PBTC-N12: A Phase II Study of [18F] FLT for PET Imaging of Brain Tumors in Children. Pediatric Brain Tumor Consortium; Grant, Frederick Daniel. (617) 355-2947

S1304: A Phase II Randomized Study Comparing Two Doses of Carfilzomib (NSC-756640) with Dexamethasone for Multiple Myeloma Patients with Relapsed or Refractory Disease. Southwest Oncology Group; Ailawadhi, Sikander. (323) 865-3913

Phase III

9355: A Pivotal Multicenter Trial of Moxetumomab Pasudotox in Relapsed/Refractory Hairy Cell Leukemia. National Cancer Institute Lab of Molecular Biology; Kreitman, Robert J. (301) 648-7375

A011202: A Randomized Phase III Trial Evaluating the Role of Axillary Lymph Node Dissection in Breast Cancer Patients (cT1-3 N1) Who Have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy. Cancer and Leukemia Group B; Boughey, Judy C. Szemere. (507) 284-8392

Other Phases

A151207: Comprehensive Molecular Characterization of Gastric and Gastroesophageal Junction Adenocarcinoma: A Collaboration with The Cancer Genome Atlas (TCGA). Cancer and Leukemia Group B; Fuchs, Charles Stewart. (617) 632-5840

AAML13B1: Evaluating the Prenatal Origin of Acute Megakaryoblastic Leukemia. Children's Oncology Group; Gruber, Tanja Andrea. (901) 595-2252

ANBL13B1: Utilizing the Immune Repertoire of Tumor Infiltrating Lymphocytes to Demonstrate Clonal Immune Responses Against Neuroblastoma (NBL). Children's Oncology Group; Maloney, Kelly Wilson. (720) 777-6673

E1900T12: Serum Metabolomics Analysis from Patients with Acute Myeloid Leukemia. Eastern Cooperative Oncology Group; Cerchietti, Leandro Carlos. (212) 746-7649

NSABP-B31-CSB: Study of SNP Markers Associated with Trastuzumab Resistance and Cardiotoxicity. National Surgical Adjuvant Breast and Bowel Project; Pogue-Geile, Katherine. (412) 359-8774

Drug Approvals

FDA Approves Bayer's Xofigo For Late-Stage Prostate Cancer

FDA approved Xofigo to treat men with symptomatic metastatic castration-resistant prostate cancer that has spread to bones, but not to other organs. The drug is intended for men whose cancer has spread after receiving medical or surgical therapy to lower testosterone.

Xofigo (radium-223 dichloride) was reviewed through the agency's priority review program, and is being approved more than three months ahead of Aug. 14, the date the agency was scheduled to complete review of the drug application.

"Xofigo binds with minerals in the bone to deliver radiation directly to bone tumors, limiting the damage

to the surrounding normal tissues," said Richard Pazdur, director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "Xofigo is the second prostate cancer drug approved by the FDA in the past year that demonstrates an ability to extend the survival of men with metastatic prostate cancer."

In August 2012, FDA approved Xtandi to treat men with metastatic castration-resistant prostate cancer that has spread or recurred, even with medical or surgical therapy to minimize testosterone. Xtandi is approved for patients who have previously been treated the chemotherapy drug docetaxel.

Xofigo's safety and effectiveness were evaluated in a single clinical trial of 809 men with symptomatic castration-resistant prostate cancer that spread to bones but not to other organs. Patients were randomly assigned to receive Xofigo or a placebo plus best standard of care.

The study was designed to measure overall survival. Results from a pre-planned interim analysis showed men receiving Xofigo lived a median of 14 months compared to a median of 11.2 months for men receiving placebo. An exploratory updated analysis conducted later in the trial confirmed Xofigo's ability to extend overall survival.

The most common side effects reported during clinical trials in men receiving Xofigo were nausea, diarrhea, vomiting and swelling of the leg, ankle or foot. The most common abnormalities detected during blood testing included low levels of red blood cells, lymphocytes, white blood cells and platelets.

Xofigo is marketed by Bayer Pharmaceuticals.

FDA approved the cobas EGFR Mutation Test, a companion diagnostic for the cancer drug Tarceva (erlotinib). This is the first FDA-approved companion diagnostic that detects epidermal growth factor receptor gene mutations, which are present in approximately 10 percent of non-small cell lung cancers.

The test is being **approved with an expanded use for Tarceva** as a first-line treatment for patients with NSCLC that has metastasized and who have certain mutations in the EGFR gene.

The safety and effectiveness of the cobas EGFR Mutation Test was established with clinical data showing that, on average, NSCLC patients with specific types of EGFR mutations (exon 19 deletions or exon 21 L858R substitution mutations) lived without their disease progressing for 10.4 months when they received Tarceva treatment, compared to 5.4 months for those who received a standard two-drug chemotherapy regimen. Investigators used tumor samples from the clinical trial to validate the test's use in this patient population.

The approval is Tarceva's fourth indication and the third use for lung cancer. The FDA approved Tarceva on April 16, 2010, for maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. Tarceva was originally approved in November 2004 for the treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.

The cobas EGFR Mutation Test is manufactured by the Roche Molecular Systems. Tarceva is co-marketed by Genentech, a member of the Roche Group, and OSI Pharmaceuticals.

FDA granted Breatkthrough Therapy Designation to daratumumab for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent, or who are double refractory to both.

Daratumumab is an investigational human monoclonal antibody with broad spectrum cytotoxic activity. It targets the CD38 molecule, which is highly expressed on the surface of multiple myeloma cells and may also have potential in other cancers on which CD38 is expressed.

It is currently in phase I/II trials for multiple myeloma and has potential applicability against other malignancies on which CD38 is expressed. Daratumumab is sponsored by Janssen Biotech Inc.

The European Commission granted an orphan drug designation to lenvatinib for the treatment of follicular and papillary thyroid cancer. The designation was also granted by the Swiss agency for therapeutic products, Swissmedic.

In the U.S., orphan drug status was granted in February 2013 by FDA in the treatment of FTC, MTC and ATC thyroid cancer. Lenvatinib is an oral tyrosine kinase inhibitor.

A phase III clinical trial, SELECT, of lenvatinib in people with RRDTC is currently underway across sites in Europe, North and South America and Asia.

Eisai Co., the drug's sponsor, has also initiated a global phase III trial with lenvatinib in hepatocellular carcinoma and is conducting phase II studies of lenvatinib in several other tumors, including endometrial cancer, melanoma and non-small cell lung cancer.