The Clinical Cancer Letter

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Leukemia

Vyxeos Injection Improves Overall Survival In Phase III Acute Myeloid Leukemia Trial

A phase III trial of Vyxeos Liposome for Injection demonstrated statistically significant improvements in overall survival in patients with high-risk secondary acute myeloid leukemia.

The median overall survival for patients treated with Vyxeos (cytarabine: daunorubicin) in the study was 9.56 months compared to 5.95 months for patients receiving the standard of care regimen of cytarabine and daunorubicin known as 7+3.

The hazard ratio was 0.69 (p=0.005) which represents a 31 percent reduction in the risk of death versus 7+3, according to Celator Pharmaceuticals Inc., the drug's sponsor, which plans to submit the data for presentation at the 2016 annual meeting of the American Society of Clinical Oncology.

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Non-Small Cell Lung Cancer

Atezolizumab Immunotherapy Boosts OS Compared to Docetaxel in Phase II Trial

Patients with advanced metastatic lung cancer treated with atezolizumab, a targeted immunotherapy drug, lived significantly longer and with fewer side effects than those who received docetaxel chemotherapy, according to a study published in The Lancet.

"The results of this study demonstrate that the use of atezolizumab, a monoclonal antibody, improves the survival rate of a majority of lung cancer patients who have progressive cancer when used after first-line chemotherapy,"

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Drugs and Targets

FDA Approves Imbruvica in First-Line CLL

FDA approved Imbruvica (ibrutinib) as a first-line treatment for patients with chronic lymphocytic leukemia.

The approval is based on data from the randomized, multi-center, open-label phase III RESONATE-2 trial, which evaluated the use of Imbruvica versus chlorambucil in 269 treatment-naïve patients with CLL or small lymphocytic lymphoma aged 65 years or older. The data were previously presented at the annual meeting of the American Society of Hematology in December 2015 and also published in The New England Journal of Medicine.

Imbruvica is jointly developed and commercialized by Pharmacyclics LLC, an AbbVie company, and Janssen Biotech Inc.

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Vyxeos Improves Survival In Phase III Leukemia Trial

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The rates of overall survival at 12 months were 41.5 percent in the Vyxeos arm compared to 27.6 percent in the 7+3 arm. At 24 months, the rates were 31.1 percent in the Vyxeos arm, and 12.3 percent in the 7+3 arm.

"The overall survival advantage seen with CPX-351 compared to 7+3, along with a superior response rate and no increase in serious toxicity indicates that we'll likely have a new standard of care for treating older patients with secondary AML," said Jeffrey Lancet, senior member and chief of the Leukemia/ Myelodysplasia Program at Moffitt Cancer Center and the principal investigator for the study. "This represents a major step forward for a very difficult-to-treat patient population."

Vyxeos also demonstrated a statistically significant improvement in induction response rate (CR+CRi of 47.7 versus 33.3 percent; p=0.016) and this significance was maintained for the analysis of CR alone (37.3 versus 25.6 percent, p=0.040). Sixty-day all-cause mortality was 13.7 percent compared to 21.2 percent.

No substantial difference in grade 3 or higher adverse events was observed between Vyxeos and 7+3. In the intent-to-treat population, grade 3 or higher hematologic adverse events were similar for overall infections, febrile neutropenia, and bleeding events. In the intent-to-treat population, grade 3 or higher non-hematologic adverse events were similar across all organ systems, including cardiac, gastrointestinal, general systems, metabolic disorders, musculoskeletal, nervous system, respiratory, skin and renal.

Based on the results, Celator plans to submit applications for Vyxeos, also known as CPX-351, with the FDA and the European Medicines Agency within the next year. The clinical trial was conducted in partnership with The Leukemia & Lymphoma Society through its Therapy Acceleration Program, which has supported the clinical development of Vyxeos since phase II.

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Non-Small Cell Lung Cancer

Atezolizumab Immunotherapy Boosts OS in Phase II Trial

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said lead author Louis Fehrenbacher, medical director of Kaiser Permanente Oncology Clinical Trials.

The phase II trial enrolled 287 patients in 13 countries between August 2013 and March 2014. All patients had metastatic non-small-cell lung cancer that had been previously treated with at least one course of chemotherapy. Genetic profiling of their tumors identified the immune-system protein PD-L1. Treatments were administered intravenously every 21 days, for as long as patients were receiving clinical benefits.

At 13 months of follow-up, patients receiving atezolizumab had an average overall survival of 12.6 months, compared to 9.7 months in the docetaxel arm. Twelve of those who received atezolizumab still had an ongoing response to the drug at that time, compared to five receiving docetaxel. At 20 months after the initiation of treatment, approximately twice as many people receiving atezolizumab survived.

Patients receiving the experimental drug were less likely to experience serious side effects than those receiving the standard chemotherapy drug, at 40.1 percent versus 52.6 percent, respectively.

Trial data showed that patients with the PD-L1 biomarker were significantly more likely to respond to the atezolizumab treatment and survive longer. Two-thirds of lung cancers in this trial expressed PDL-1 on either their cancer cells or immune cells.

Atezolizumab is an experimental drug developed by Roche and Genentech, which sponsored the clinical trial. Atezolizumab is not approved by the FDA.

Abraxane Trial Demonstrates Improved Quality of Life

Two interim analyses of an ongoing phase III trial of Abraxane demonstrated that exploratory quality of life measures were maintained or improved in patients with advanced squamous non-small cell lung cancer.

The study, ABOUND.sqm, is evaluating initial treatment with Abraxane (paclitaxel protein-bound particles for injectable suspension; albumin-bound) in combination with carboplatin. The analyses were presented at the 2016 ASCO Quality Care Symposium.

In the study, patients received four 21-day cycles of Abraxane (100 mg/m2 on days 1, 8 and 15) plus carboplatin (AUC6 on day 1) and those with a response or stable disease could be randomized to receive either Abraxane (100 mg/m2 on days 1, 8) plus best supportive care or best supportive care alone in 21-day cycles until disease progression.

The analyses included 159 patients from the study who were evaluable for radiological response and quality of life. In the two analyses, 99 percent of patients had an ECOG performance status of 0-1 and pre-defined QoL measures including the LCSS (Global Score, Average Total Score, 3-Item Index, Average Symptom Burden Index and Lung Cancer Symptoms) and EuroQol EQ-5D-5L assessment were taken on day one of each cycle during the initial treatment phase.

The first analysis evaluated the therapeutic impact of chemotherapy on patient symptoms and activities. For all patients in the analysis, quality of life as measured by the LCSS and EuroQoL (EQ-5D-5L) was generally either maintained or improved throughout the entire treatment course, according to Celgene Corp., the sponsor of the study.

The second analysis assessed the impact of radiological response on quality of life. In this analysis, 93 of 159 patients had an unconfirmed radiological response, and 66 did not. Responders had a greater improvement in lung cancer symptom score, as measured by the LCSS and EQ-5D-5L scores.

Among patients who reported problems with mobility, self-care, usual activities of living, pain/discomfort, or anxiety/depression prior to treatment, 38 to 47 percent reported complete resolution of these problems at least once during treatment.

This was more pronounced in patients who achieved a radiological response, with complete resolution at least once reported in 42 to 59 percent of patients.

Abraxane is indicated for the first-line treatment of locally advanced or metastatic non–small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.

Ovarian Cancer

Study: Reolysin-Paclitaxel Combination Demonstrates Higher Response Than Paclitaxel Therapy Alone

Updated results from a phase II trial of Reolysin and paclitaxel in ovarian cancer patients showed that an intent-to-treat analysis of tumor response, as assessed by CA-125 antigen levels, demonstrated statistically significantly higher full response rates and stable disease or better rates in the test arm compared to paclitaxel alone.

The rate of full responses in the combination arm was 9.26 percent, compared to 1.85 percent in the control arm ($p = 0.0196$). The rate of stable disease or better in the test arm was 44.44 percent, compared with 24.08 percent in the control arm ($p = 0.0096$).

Response rates as measured by RECIST were performed on patients with measurable disease (n=68, out of 108 total). The proportion responding on the test arm was 17 percent compared to 20 percent in the control arm.

The study, GOG-0186H, is a randomized clinical trial of paclitaxel versus paclitaxel plus Reolysin in patients with persistent or recurrent ovarian, fallopian tube or primary peritoneal cancer. The update follows a presentation of the study at the Society of Gynecologic Oncology's Annual Meeting on Women's Cancer. The study was sponsored by the NCI and conducted by the former GOG, now incorporated into NRG Oncology.

An analysis of progression free survival stratified by measurable disease and platinum-free interval (test arm: n=54, 43 progressions, and control arm: n = 54, 48 progressions) was performed and demonstrated a median PFS of 4.4 months for the test arm, and 4.3 months for the control arm.

An interim analysis of overall survival (test arm: n=54, 32 deaths, and control arm: n=54, 32 deaths) was performed and demonstrated a median OS of 12.9 months for the test arm, and 15.0 months for the control arm.

The OS was an interim analysis, as 41 percent of patients were alive at the time of analysis. Given the

number of patients still alive on the test and control arms with current survival less than the median, final median OS results are expected to change, according to Oncolytics Biotech Inc., Reolysin's sponsor.

"This is one of a total of six randomized phase II studies with Reolysin that were designed and sponsored by third parties. The results from these studies will determine clinical targets, endpoints, and study designs for follow on and registration studies conducted by Oncolytics. In the case of this ovarian cancer study, we are pleased that Reolysin has demonstrated a statistically significant reduction in tumor burden in ovarian cancer patients as measured by CA-125 levels," said Brad Thompson, president and CEO of Oncolytics.

"This adds to our results in other indications that have shown improvement in tumor responses. In order to further our understanding of how Reolysin interacts with the immune system, we hope, in conjunction with the principal investigator, to analyze the PD-1 and CD8(+) T lymphocyte levels of patients on entry and correlate these with overall survival and progression free survival."

The study did not stratify on entry according to PD-L1 levels or infiltrating CD8(+) T lymphocyte levels, nor were either of those levels measured post-treatment. However, pre-treatment tumor biopsies were taken from the majority of patients, according to Oncolytics.

Glioblastoma

Tocagen Expands Phase II/III Trial, Begins Enrolling in Canada

Tocagen Inc. expanded its phase II/III clinical trial Toca 5, and is now enrolling patients in Canada. The trial first began enrolling patients in the U.S. in December 2015.

The study compares the combination of Toca 511 (vocimagene amiretrorepvec) and Toca FC (extended-release 5-fluorocytosine) to standard of care in patients with first or second recurrence of glioblastoma or anaplastic astrocytoma who are undergoing resection.

The study's primary endpoint is overall survival. Investigators may choose chemotherapy (lomustine or temozolomide) or antiangiogenic therapy (bevacizumab) for the control arm.

"With enrollment ongoing in the United States, expanding the study to include patients in Canada is an important milestone for the Canadian brain tumor community as well as for Tocagen," said Jamey Skillings, chief medical officer of Tocagen. "We are grateful to the various individuals and groups who contributed to this achievement, and we look forward to opening additional sites internationally as we continue to advance this potential new treatment option for patients with high grade glioma."

The Canadian Brain Tumour Consortium is facilitating the Toca 5 trial in Canada under the consortium's chair, James Perry, who is head of division of neurology at Sunnybrook Health Sciences Centre at the University of Toronto.

Tocagen's cancer-selective gene therapy platform is built on retroviral replicating vectors (RRVs) which are designed to selectively integrate into the DNA of cancer cells which then serve as factories for these RRVs to replicate and infect neighboring cancer cells, providing long-term presence of the therapeutic gene(s).

Toca 511 is a proprietary injectable retroviral replicating vector that encodes the prodrug activator enzyme cytosine deaminase. Toca FC is an orally administered, proprietary extended-release version of 5-fluorocytosine, a prodrug that is inactive as an anti-cancer drug. Toca FC is converted into the active anti-cancer drug, 5-fluorouracil, at high concentrations in Toca-511-infected cancer cells that are producing CD protein.

5-FU is a well-established anti-cancer agent used effectively in many conventional chemotherapy settings. According to Tocagen, the treatment is designed for 5-FU to kill neighboring uninfected cancer cells and myeloid derived suppressor cells in the tumor microenvironment, activating the immune system against the patient's cancer antigens.

Cachexia

Two Phase III Anamorelin Trials Show Improved Lean Body Mass

Two phase III trials in non-small cell lung cancer patients with cachexia found that treatment with anamorelin significantly improved lean body mass and body weight compared to placebo, in addition to improving symptom burden, including appetite. No differences in handgrip strength were observed, one of the co-primary endpoints of the study.

Most participants in the trials were receiving chemotherapy. Improvements in patients' weight and symptom burden were observed as early as three weeks and progressive, according to Helsinn, which

sponsored the studies. The two studies, ROMANA 1 and ROMANA 2, were published in The Lancet Oncology.

The international, double-blind trials evaluated the efficacy and safety of anamorelin in patients with stage III/IV NSCLC and cachexia (greater than or equal to 5 percent weight loss within six months or BMI <20 kg/m[2]).

ROMANA 1 enrolled 484 patients and ROMANA 2 enrolled 495 patients. Patients were randomized 2:1 to 100 mg anamorelin or placebo, given daily orally for 12 weeks, and were permitted to receive chemotherapy while on study.

Efficacy was assessed through change from baseline in the co-primary endpoints, lean body mass (measured by dual-energy X-ray absorptiometry) and handgrip strength, and in the secondary endpoints, which included body weight, and the anorexia-cachexia symptoms and concerns.

Over 12 weeks, anamorelin significantly increased median lean body mass versus placebo in ROMANA 1 (0.99 vs -0.47 kg; $p<0.001$) and ROMANA 2 (0.65 vs -0.98 kg; $p<0.0001$).

Anamorelin-treated patients also significantly improved compared to placebo Cancer Anorexia-Cachexia symptoms and concerns (ROMANA 1: 4.12 vs 1.92; $p=0.0004$; and ROMANA 2: 3.48 vs 1.34; $p= 0.0016$), and significantly gained body weight (ROMANA 1: 2.20 vs 0.14 kg; $p<0.0001$; and ROMANA 2: 0.95 vs -0.57 kg; $p<0.0001$).

There were no differences in grade 3-4 drug-related adverse events between study arms. Hyperglycemia was the most common grade 3-4 drug-related adverse event occurring in less than or equal to 1 percent of patients receiving anamorelin.

Anamorelin HCl is an ghrelin receptor agonist that is under development for the treatment of Anorexia, Cachexia, and Unintended Weight Loss in NSCLC patients. Ghrelin is an endogenous peptide primarily secreted by the stomach. Upon binding to its receptor, ghrelin stimulates multiple pathways in the positive regulation of body weight, lean body mass, appetite and metabolism, according to Helsinn.

Anamorelin has not yet been approved by any regulatory authority; a marketing authorization application is under review by the European Medicines Agency.

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NCI CTEP-Approved Trials For the Month of March

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

10004: A Phase I Study of Subcutaneous Recombinant Human IL-15 (S.C. Rhil-15) and Alemtuzumab for Patients with Refractory or Relapsed Chronic and Acute Adult T-Cell Leukemia (ATL). NCI Center for Cancer Research; Waldmann, Thomas Alexander. (301) 496-6656

9882: Phase I and Pharmacology Study of Oral 5-Iodo-2-Pyrimidinone-2'- Deoxyribose (IPdR) as a Prodrug for IUdR-Mediated Tumor Radiosensitization in Gastrointestinal Cancers. Rhode Island Hospital; Kinsella, Timothy James. (401) 444-6203

Phase II

AOST1521: A Phase 2 Study of GPNMB-Targeted Antibody-Drug Conjugate, CDX-011 (Glembatumumab Vedotin, CR011-vcMMAE; IND# 128248, NSC# 763737), in Recurrent or Refractory Osteosarcoma. Children's Oncology Group; Kopp, Lisa M. (520) 626-2021

Other Phases

AALL15B2-Q: Use of DNA Methylation Assessment by xMELP for Prognosis in Pediatric Patients with T-ALL. Children's Oncology Group; Wertheim, Gerald. (267) 970-5918

AALL15B7-Q: Role of the MAPK/ERK Pathway in Relapsed Pediatric B-Lymphoblastic Leukemia: Prognostic Implications and Potential for Targeted Therapy. Children's Oncology Group; Carroll, William L. (212) 263-9947

ANHL15B1-Q: B-Lineage Lymphoblastic Lymphoma SNP Array Profiling. Children's Oncology Group; Miles, Rodney R. (801) 213-3448

AREN15B2-Q: Mapping Endogenous Mobile Elements in Rhabdoid Tumors. Children's Oncology Group; Kentsis, Alex. (646) 888-2593

ARST15B2-Q: Validation of Anti-FGFR4 Antibodies as Potential Therapeutic Agents for Rhabdomyosarcoma. Children's Oncology Group; Khan, Javed. (301) 439-2937

ARST15B4-Q: Infantile Rhabdomyosarcoma. Children's Oncology Group; Arnold, Michael Andrew. (614) 722-5719

S1415CD: A Pragmatic Trial to Evaluate a Guideline-Based Colony Stimulating Factor Standing Order Intervention and to Determine the Effectiveness of Colony Stimulating Factor Use as Prophylaxis for Patients Receiving Chemotherapy with Intermediate Risk for Febrile Neutropenia-Pragmatic Traisl Assessing CSF Prescribing Effectiveness and Risk (TRACER). SWOG; Ramsey, Scott David. (206) 667-7846

Drugs and Targets

FDA Approves Imbruvica as First-Line CLL Therapy

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Imbruvica is now approved to treat CLL patients regardless of their treatment history, as well as to treat high-risk CLL patients with del17p. This is the fifth treatment indication for Imbruvica.

RESONATE-2 showed Imbruvica significantly improved progression-free survival and overall response rate compared to chlorambucil in treatment-naïve patients aged 65 or older with CLL or small lymphocytic lymphoma. The data indicated an 84 percent reduction in the risk of death or progression in the Imbruvica arm versus the chlorambucil arm (HR=0.161 [95% CI, 0.091-0.283]). Median PFS was not reached for Imbruvica, versus 18.9 months for chlorambucil (95 percent CI: 14.1, 22.0).

FDA approved Xalkori (crizotinib) to treat people with metastatic non-small cell lung cancer whose tumors have an ROS-1 gene alteration. Xalkori, sponsored by Pfizer, is the first and only FDA approved treatment for patients with ROS-1 positive NSCLC. FDA previously granted the Xalkori expanded use application breakthrough therapy designation and priority review status.

ROS-1 gene alterations are present in approximately 1 percent of patients with NSCLC. The overall patient and disease characteristics of NSCLC with ROS-1 gene alterations appear similar to NSCLC with anaplastic lymphoma kinase gene alterations, for which crizotinib use was previously approved. Xalkori was approved to treat certain patients with late-stage NSCLC that expresses an abnormal ALK gene in 2011.

"Lung cancer is difficult to treat, in part, because patients have different mutations, some of which are rare," said Richard Pazdur, director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "The expanded use of Xalkori will provide a valuable treatment option for patients with the rare and difficult to treat ROS-1 gene mutation by giving health care practitioners a more personalized way of targeting ROS-1 positive NSCLC."

The safety and efficacy of Xalkori for the treatment of patients with ROS-1 positive tumors were evaluated in a multi-center, single-arm study of 50 patients with ROS-1 positive metastatic NSCLC. Results showed 66 percent of participants experienced a complete or partial shrinkage of their NSCLC tumors, an effect that lasted a median of 18.3 months. The safety results of this study were generally consistent with the safety profile of Xalkori evaluated in 1,669 patients with ALK-positive metastatic NSCLC.

FDA approved Defitelio (defibrotide sodium) to treat adults and children who develop hepatic veno-occlusive disease with additional kidney or lung abnormalities after hematopoietic stem cell transplantation. This is the first FDA-approved therapy for treatment of severe hepatic VOD. Hepatic VOD can occur in patients who receive chemotherapy and HSCT.

The efficacy of Defitelio was investigated in 528 patients treated in three studies: two prospective clinical trials and an expanded access study. The patients enrolled in all three studies had a diagnosis of hepatic VOD with liver or kidney abnormalities after HSCT.

In the three studies, 38 to 45 percent of patients treated with Defitelio were alive 100 days after HSCT. Based on published reports and analyses of patient-level data, the expected survival rates 100 days after HSCT would be 21 to 31 percent for patients with severe hepatic VOD who received only supportive care or interventions other than Defitelio.

The most common side effects of Defitelio include abnormally low blood pressure, diarrhea, vomiting, nausea and nosebleeds. Serious potential side effects of Defitelio that were identified include bleeding and allergic reactions. Defitelio should not be used in patients who are having bleeding complications or who are taking blood thinners or other medicines that reduce the body's ability to form clots.

The FDA previously granted Defitelio priority review and an orphan drug designation. Defitelio is marketed by Jazz Pharmaceuticals.

FDA is alerting health care professionals about reports of an increased rate of adverse events, including deaths, in clinical trials with the cancer medicine Zydelig (idelalisib) in combination with other cancer medicines.

Gilead Sciences Inc. stopped six clinical trials involving Zydelig, in patients with chronic lymphocytic leukemia, small lymphocytic lymphoma and indolent non-Hodgkin lymphomas. The FDA said it is reviewing the findings of the clinical trials and will communicate new information as necessary. Health care professionals should be aware that Zydelig is not approved for previously untreated chronic lymphocytic leukemia, the agency said.

The FDA is urging health care professionals and patients to report adverse events involving Zydelig to the FDA MedWatch program.

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee issued provisional advice for doctors and patients, while the medicine is being reviewed, to ensure that it continues to be used as safely as possible. Zydelig is currently authorized in the EU to treat chronic lymphocytic leukemia and follicular lymphoma.

The committee recommends that all patients treated with Zydelig should receive antibiotics to prevent a particular type of lung infection, Pneumocystisjirovecii pneumonia. Patients should also be monitored for infection and have regular blood tests for white cell counts because low counts can increase their risk of infection. Zydelig should not be started in patients with a generalized infection. It should also not be started in previously untreated patients with CLL whose cancer cells have certain genetic mutations (17p deletion or TP53 mutation), the committee said.

Zydelig is currently approved by the FDA for the treatment of relapsed chronic lymphocytic leukemia, in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities; relapsed follicular B-cell non-Hodgkin lymphoma in patients who have received at least two prior systemic therapies; and relapsed small lymphocytic lymphoma in patients who have received at least two prior systemic therapies.

FDA approved the American College of Radiology's alternative standard request to allow mammography facilities to use the new Digital Mammography Quality Control Manual and Digital Mammography QC Phantom in routine QC of digital equipment. The new manual and phantom will aid in ensuring uniformity of QC testing, the ACR said.

The FDA alternative standard specifies that the new manual may only be used for full-field digital mammography systems without advanced imaging capabilities, such as tomosynthesis or contrast enhancement.

"The new ACR manual will promote uniformity of testing since it will allow facilities with applicable systems to follow one manual instead of the dozens of different manuals that are mandated for the varying manufacturers and models of digital mammography equipment," said Eric Berns, lead author and chair of the ACR Subcommittee on Mammography Quality Assurance. "The new manual focuses on tests that are clinically relevant for high-quality imaging and the structure for a thorough and complete quality control program," he added.

The manual is currently undergoing preparation for publication and should be available this spring. ACR-accredited mammography facilities (and those applying for accreditation) will be invited to download the PDF manual at no charge. Medical physicists associated with ACR-accredited facilities will also be allowed to download the manual at no charge.

"This new manual provides simple, user-friendly procedures for technologists and medical physicists to help them maintain this quality of imaging," said Brett Parkinson, chair of the ACR Committee on Mammography Accreditation. He noted that the ACR manual "also contains two optional procedures for radiologists to enable them to self-check system image quality and provide image quality feedback to technologists."

Regulatory authorities in six countries have granted 10 sales authorizations for Yondelis.

Five of those authorizations are for Yondelis (trabectedin) in combination with Caelyx (pegylated liposomal doxorubicin) for treating relapsed platinum-sensitive ovarian cancer, in Bangladesh, Costa Rica, Kuwait, Moldavia and Saudi Arabia

The other five authorizations are for Yondelis for soft tissue sarcoma, in Bangladesh, Brunei, Kuwait, Moldavia and Saudi Arabia

As a result, Yondelis is now approved in nearly 80 countries, 31 of which are in the European Economic Area. The European Commission approved Yondelis for soft tissue sarcoma in 2007, and at the end of 2009

they approved the sale of this drug in combination with Caelyx for relapsed platinum-sensitive ovarian cancer.

In 2015, the FDA gave Janssen Products LP marketing approval for Yondelis for the treatment of patients with unresectable or metastatic liposarcoma or leiomyosarcoma; and the drug was also approved by the Japanese Minister of Health, Labor and Welfare to Taiho Pharmaceutical Co., Ltd. for the treatment of patients with soft tissue sarcoma.

Yondelis also has orphan drug status for soft tissue sarcoma and ovarian cancer in the European Union, the United States, and Switzerland, and for soft tissue sarcoma in Japan and South Korea.

According to the licensing agreement between Janssen Products and PharmaMar, PharmaMar has the rights to sell Yondelis in Europe, including Eastern Europe, while Janssen Products has the rights to sell the drug everywhere else except Japan, where PharmaMar has granted a license to Taiho Pharmaceutical Co., Ltd.

Yondelis is a novel, multimodal, synthetically produced antitumor agent, originally derived from the sea squirt, Ecteinascidia turbinata. The drug exerts its activity by targeting the transcriptional machinery and impairing DNA repair.

Health Canada approved Opdivo injection (nivolumab), the first and only immuno-oncology therapy approved in Canada for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with progression on or after platinum-based chemotherapy.

The approval was made under the Health Canada Priority Review process, after having met the criteria of substantial evidence of clinical effectiveness providing an improved benefit/risk profile over existing therapies. The data to support the approval was based on CheckMate-017 and CheckMate-057 trials and both phase three trials were stopped early when an independent data review showed evidence of superior overall survival in patients receiving Opdivo over chemotherapy treatment.

The results of the CheckMate-017 trial demonstrated superior overall survival in previously treated metastatic, squamous-cell NSCLC compared to chemotherapy, with a 41 percent reduction in the risk of death.

Opdivo-treated patients lived 3.2 months longer, with the median OS at 9.2 months in the Opdivo arm (95% CI: 7.3, 13.3) and 6.0 months in the docetaxel arm (95% CI: 5.1, 7.3). A one-year OS rate showed survival was almost double of that compared to docetaxel chemotherapy, 42 percent (n=135, 95% CI: 34-50) vs 24 percent (n=137, 95% CI =17-31).

In CheckMate-057, Opdivo demonstrated superior overall survival in previously treated metastatic non-squamous NSCLC compared to chemotherapy, with a 27 percent reduction in the risk of death. Opdivo-treated patients lived 2.8 months longer, with the median OS at 12.2 months in the Opdivo arm (95% CI: 9.7, 15.0) and 9.4 months in the docetaxel arm (95% CI: 8.0, 10.7). The overall survival rate at one year was 51 percent (95% CI, 45 to 56) with Opdivo and 39 percent (95% CI, 33 to 45) with docetaxel.

Treatment-related adverse events occurred less frequently with Opdivo than docetaxel. The most frequently reported drug-related AEs were fatigue, nausea, rash and decreased appetite in patients treated with Opdivo.

Opdivo was first approved in September 2015 for the treatment of adult patients with metastatic BRAF V600 wild-type melanoma. Opdivo currently has regulatory approval in 46 countries including the U.S., Japan, and in the European Union.

The China Food and Drug Administration approved the CINtec PLUS Cytology test, developed by Roche, for identifying women with cervical pre-cancer.

A multi-center study of five participating hospitals throughout China revealed greater overall performance of combined sensitivity and specificity of the CINtec PLUS Cytology test in determining which women are at higher risk of developing cervical cancer when compared to conventional screening methods like Pap cytology. This is consistent with previously published data and supported the approval of the test by the CFDA.

The CINtec PLUS Cytology test was developed to detect two biomarkers associated with persistent HPV infections that may lead to cancer, distinguishing them from those that are likely to resolve on their own. The test is also available in Europe, Asia, Latin America and Canada.

FDA granted orphan drug designation for Iomab-B, a radioimmunotherapeutic that conditions relapsed and refractory acute myeloid leukemia patients for a hematopoietic stem cell transplant. Actinium Pharmaceuticals Inc., iomab-B's sponsor, plans to begin a phase III trial in 150 relapsed and refractory AML patients over the age of 55.

Iomab-B is a radioimmunoconjugate consisting of BC8, a novel murine monoclonal antibody, and

iodine-131 radioisotope. BC8 has been developed by the Fred Hutchinson Cancer Research Center to target CD45, a pan-leukocytic antigen widely expressed on white blood cells.

This antigen makes BC8 potentially useful in targeting white blood cells in preparation for hematopoietic stem cell transplantation in a number of blood cancer indications, including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, Hodgkin's disease, Non-Hodgkin lymphomas and multiple myeloma. When labeled with radioactive isotopes, BC8 carries radioactivity directly to the site of cancerous growth and bone marrow while avoiding effects of radiation on most healthy tissues.

FDA granted orphan drug designation to the WT1 cancer vaccine developed by SELLAS Life Sciences Group for the treatment of patients with malignant pleural mesothelioma.

SELLAS recently reported positive results of a phase II trial of its WT1 vaccine in MPM patients, showing that overall survival improved and progression-free survival doubled. Based on these findings, SELLAS intends to initiate a phase IIb/III trial of its product candidate in patients with MPM by the third quarter of this year.

"We are thrilled with the progress of our WT1 vaccine program, which has received two orphan designations in the last two months and is advancing into pivotal studies in AML and in MPM patients in 2016, as well as further phase II studies including in multiple myeloma, ovarian cancer, glioblastoma multiforme, and a series of genetically defined cancers in a basket-trial design," said Angelos Stergiou, chairman and CEO of SELLAS.

The European Medicines Agency granted an Orphan Drug Designation to venetoclax, an investigational, oral B-cell lymphoma-2 inhibitor, for the treatment of acute myeloid leukemia. Venetoclax is being developed by AbbVie in partnership with Genentech and Roche.

The EMA previously granted Orphan Drug Designation to venetoclax for the treatment of chronic lymphocytic leukemia. Orphan Designation is granted to therapies aimed at the treatment, prevention or diagnosis of life-threatening diseases that affect no more than five in 10,000 persons in the European Union and for which no satisfactory therapy is available.

"There have been very few treatment advances for patients with AML who are older than 60, the patient population that is most often affected by this aggressive and life-threatening cancer," said Michael Severino, executive vice president of research and development and chief scientific officer at AbbVie.

FDA recently granted venetoclax both Breakthrough Therapy Designation and Orphan Drug Designation for the treatment of patients with AML. The FDA has also granted venetoclax Breakthrough Therapy Designation for the treatment of CLL in previously treated patients with the 17p deletion genetic mutation and in combination with rituximab for the treatment of patients with relapsed/refractory chronic lymphocytic leukemia.

Additionally, venetoclax recently received validation from the EMA for its Marketing Authorization Application for the treatment of CLL patients with 17p deletion or TP53 mutation, as well as acceptance by Health Canada for the New Drug Submission for the treatment of patients with CLL who have received at least one prior therapy, including patients with 17p deletion.

The BCL-2 protein prevents apoptosis of some cells, including lymphocytes, and can be over expressed in some cancer types. Venetoclax is designed to selectively inhibit the function of the BCL-2 protein. Venetoclax is currently being evaluated in phase III clinical trials for the treatment of relapsed/refractory CLL, along with studies in several other cancers.

FDA granted an Orphan Drug Designation to VAL-083 for the treatment of medulloblastoma. The investigational drug candidate, developed by DelMar Pharmaceuticals Inc., previously received an orphan designation for glioblastoma in the U.S. and in Europe.

VAL-083 is a first-in-class chemotherapeutic. In more than 40 phase I and II clinical studies sponsored by the NCI, VAL-083 demonstrated clinical activity against a range of cancers including lung, brain, cervical, ovarian tumors and leukemia both as a single-agent and in combination with other treatments.

In historical NCI-sponsored clinical studies, VAL-083 demonstrated clinical activity against medulloblastoma. In these studies VAL-083 was investigated both as a stand-alone therapy and in combination with other chemotherapeutic regimens. DelMar's recent pre-clinical research demonstrates that VAL-083 is active against medulloblastoma cells with difficult to treat sonic hedgehog characteristics and p53 mutations; and VAL-083 in combination with temozolomide completely inhibits self-renewal

of pediatric brain cancer stem cells.

Additionally, DelMar has been conducting clinical trials with VAL-083 as a potential treatment for glioblastoma multiforme. In September 2015, DelMar announced completion of enrollment in a phase II clinical trial in refractory GBM. The company anticipates top-line overall survival data from this trial in the first half of this year.

FDA granted Priority Review for atezolizumab (anti-PDL1; MPDL3280A) for the treatment of people with locally advanced or metastatic urothelial carcinoma who had disease progression during or following platinum-based chemotherapy in the metastatic setting, or whose disease worsened within 12 months of receiving platinum-based chemotherapy before or after surgery.

"Atezolizumab was granted Priority Review designation based on results of the IMvigor 210 study, which showed the medicine shrank tumors in a type of advanced bladder cancer, and the majority responding to treatment continued to respond after nearly a year of follow up," said Sandra Horning, chief medical officer and head of Global Product Development at Genentech, the drug's sponsor. "The treatment options available for advanced bladder cancer are very limited, and we are committed to working with the FDA to bring the first anti-PDL1 cancer immunotherapy to people with this disease as quickly as possible."

IMvigor 210 is an open-label, multicenter, single-arm phase II study that evaluated the safety and efficacy of atezolizumab in people with locally advanced or mUC, regardless of PD-L1 expression. People in the study whose disease had progressed during or following previous treatment with a platinum-based chemotherapy regimen (n=311) received a 1200-mg intravenous dose of atezolizumab on day one of 21-day cycles until loss of clinical benefit. The primary endpoint of the study was objective response rate as assessed by an independent review facility. Secondary endpoints included duration of response, overall survival, progression-free survival and safety.

In an updated analysis based on 11.7 months of median follow up, atezolizumab shrank tumors in 15 percent (95% CI: 11, 19) of people evaluable for efficacy and safety (n=310) whose disease progressed after platinum-based chemotherapy.

Atezolizumab shrank tumors in 26 percent (95% CI: 18, 36) of people whose disease had medium and high levels of PD-L1 expression. Median duration of response was not reached at the time of analysis; with a median duration of follow up of 11.7 months, 84 percent of people had an ongoing response.

Genentech also has an ongoing, confirmatory phase III study (IMvigor 211), which compares atezolizumab to chemotherapy in people whose bladder cancer has progressed on at least one prior platinum-containing regimen.

FDA approved a hepatitis C virus quantitative RNA test to be used as an aid in the diagnosis of HCV infection for certain patient populations.

Results from the COBAS AmpliPrep/COBAS TaqMan HCV Test v2.0, developed by Roche, can now be used to confirm an active hepatitis infection, in addition to providing an accurate measurement of how much virus is in a patient's blood, to help a physician determine the best course of treatment.

The test is the first quantitative HCV RNA test to be approved for use as an aid in diagnosis for active HCV infection. This expanded indication is in addition to its approved use as a viral load test to help physicians assess a patient's response to antiviral therapy. Roche HCV viral load tests have also been used to establish the treatment efficacy of direct-acting antiviral treatment regimens recently approved by the FDA.

The dual-probe PCR assay is intended for use in the management of patients with chronic HCV, in conjunction with clinical and laboratory markers of infection, and as an aid in diagnosis for individuals with antibody evidence of HCV infection with evidence of liver disease, individuals suspected to be actively infected with HCV antibody evidence, and individuals at risk for HCV infection with antibodies to HCV. Detection of HCV RNA indicates that the virus is replicating and therefore is evidence of active infection.

The test is an in vitro nucleic acid amplification test for the detection and quantitation of hepatitis C virus RNA genotypes 1 to 6 in human EDTA plasma or serum. It can be used to predict the probability of sustained virologic response early during a course of antiviral therapy and to assess viral response to antiviral treatment, as measured by changes of HCV RNA levels.