The Clinical Cancer Letter

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Non-Small Cell Lung Cancer

Pooled Analysis of Two LUX-Lung Trials Shows Prolonged Survival with Afatinib

New overall survival data of two phase III clinical trials, LUX-Lung 3 and LUX-Lung 6, demonstrated that patients with advanced non-small cell lung cancer whose tumors have the most common epidermal growth factor receptor mutation lived longer if treated with first-line afatinib compared to chemotherapy.

In the pooled analysis, afatinib (Gilotrif) prolonged survival of lung cancer patients whose tumors have common EGFR mutations compared with standard chemotherapy by a median of 3 months (27.3 to 24.3 months) and significantly reduced the risk of death by 19 percent (HR=0.81, p=0.037).

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Prostate Cancer

Enzalutamide Reduced Risk of Progression By 81 Percent in Metastatic Prostate Cancer

A drug used to treat men with late-stage prostate cancer proved effective in stemming progression of the disease in research participants who had not yet received chemotherapy and extended their survival, according to results from a multi-national phase III clinical trial

An analysis of the study's results, published in the New England Journal of Medicine and presented at the American Society of Clinical Oncology annual meeting in Chicago, found that participants treated with enzalutamide saw an 81 percent reduction in the risk the cancer would progress and a 29 percent reduction in the risk of death.

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Pancreatic Cancer

Vaccine and LDCT Pretreatment Can Help PDACs Become Vulnerable to Immunotherapy

By priming pancreatic ductal adenocarcinomas with a therapeutic vaccine and a low-dose chemotherapy combination prior to surgery, researchers converted PDACs into cancers that may respond to immunotherapy.

Researchers pretreated PDAC patients with the vaccine GVAX and low doses of the chemotherapy cyclophosphamide, which caused the aggregation of immune cells inside the patients' tumors, and many of these immune cells expressed proteins that may make these cancers amenable to immunotherapies such as PD-1 inhibitors.

The trial was published in Cancer Immunology Research, a journal of the American Association for Cancer Research, produced in collaboration with the Cancer Research Institute).

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EGFR Exon 19 Deletion Patients Responded Best to Afatinib

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The most pronounced reduction in risk of death was 41 percent (HR=0.59, CI 0.45, 0.77), in patients whose tumors have the most common EGFR mutation, exon 19 deletion. For patients with the exon 21 (L8585R) mutation there was no impact on overall survival (HR=1.25, CI 0.92, 1.71). Exon 19 deletions occur with a frequency of approximately 48 percent in EGFR-mutant lung tumors.

The new data was presented June 2 at the annual meeting of the American Society of Clinical Oncology in Chicago. The analysis of the delay in tumor growth and adverse events associated with afatinib in comparison with standard chemotherapy were consistent with previously published results of the primary data from these two trials.

The LUX-Lung 3 trial compared afatinib with pemetrexed/cisplatin chemotherapy as a first-line treatment in patients with advanced NSCLC with EGFR mutations. LUX-Lung 6 clinical trial evaluated afatinib versus gemcitabine/cisplatin chemotherapy as a first-line treatment for Asian patients with advanced NSCLC with EGFR mutations.

Results from a third phase III study in NSCLC patients—LUX-Lung 5, which was also presented at ASCO—met its primary endpoint by showing an improvement in progression-free survival when continuing treatment with afatinib in combination with chemotherapy after the tumor started to grow on afatinib alone. This study compared afatinib and paclitaxel versus investigator's choice of chemotherapy alone in patients with late-stage NSCLC whose disease has progressed after afatinib alone and have also failed several treatments, including chemotherapy, erlotinib or gefitinib.

Those patients who continued afatinib treatment, with the addition of chemotherapy, after progressing on afatinib alone, had a further delay in tumor growth compared to the group who stopped afatinib treatment and received chemotherapy only—tumor growth was delayed by 5.6 months and 2.8 months, respectively (p=0.003). This corresponded to a 40 percent reduction in risk of disease progression (HR=0.60).

Afatinib is an oral, once-daily kinase inhibitor, sponsored by Boehringer Ingelheim, and indicated for the first-line treatment of patients with metastatic non-small cell lung cancer whose tumors have epidermal growth factor receptor exon 19 deletions or exon 21 substitution mutations as detected by an FDA-approved test.

Cyramza-Docetaxel Combination Extends OS In Second-Line NSCLC

A phase III trial of Cyramza in combination with chemotherapy significantly improved overall survival in patients with second-line non-small cell lung cancer.

The global, randomized, double-blind trial compared Cyramza plus docetaxel to placebo plus docetaxel in NSCLC patients with progression after platinum-based chemotherapy for locally-advanced or metastatic disease.

The study included a total of 1,253 nonsquamous and squamous NSCLC patients from 26 countries on six continents. Overall survival was the trial's primary endpoint and secondary endpoints included progression-free survival and objective response rate.

Patients treated on the Cyramza-docetaxel arm (n=628) achieved a median OS of 10.5 months compared to 9.1 months for patients on the placebo-docetaxel arm (n=625). The OS hazard ratio was 0.86 (95% CI, 0.751-0.979, p=0.023), which corresponds to a 14 percent reduction in risk of death.

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Median PFS was 4.5 months in the Cyramza arm compared to 3.0 months in the placebo arm, with a PFS hazard ratio of 0.76 ($p<0.001$), which corresponds to a 24 percent reduction in risk of progression or death. Overall response rate was 23 percent with Cyramza and 14 percent on placebo ($p<0.0001$).

The study, named REVEL, was published in The Lancet and presented at the American Society of Clinical Oncology Annual Meeting June 2. REVEL is the first positive phase III study of a biologic in combination with chemotherapy to demonstrate improved overall survival compared to chemotherapy alone in second-line NSCLC.

"While there have been other recent phase III studies that have evaluated the addition of a cytotoxic or targeted agent in previously-treated NSCLC patient populations, none have demonstrated improved overall survival in the total patient population," said Richard Gaynor, senior vice president of product development and medical affairs for Lilly Oncology, the drug's sponsor.

"We are pleased that Cyramza demonstrated a significant survival improvement in a difficult-to-treat patient population where there continues to be a major unmet medical need in both nonsquamous and squamous NSCLC patients. [These data] also add to our growing clinical data set for Cyramza, which is being studied in multiple tumor types."

Lilly intends to submit the first application of these data to regulatory authorities in the second half of 2014, according to the sponsor.

Cyramza as a single agent is approved for patients with advanced gastric cancer or gastroesophageal junction adenocarcinoma who have progressed after prior fluoropyrimidine- or platinum-containing chemotherapy. Cyramza is a VEGF Receptor 2 antagonist that specifically binds and blocks activation of VEGF Receptor 2 and blocks binding of VEGF receptor ligands VEGF-A, VEGF-C, and VEGF-D.

Leukemia

Ibrutinib Increases OS, PFS Versus Ofatumumab in Phase III

Data from the phase III RESONATE trial showed that monotherapy ibrutinib significantly lengthened progression-free survival and overall survival compared to ofatumumab in relapsed or refractory chronic lymphocytic leukemia or small lymphocytic leukemia.

The trial results were presented at the annual meeting of the American Society of Clinical Oncology June 3 and were simultaneously published in The New England Journal of Medicine.

The median PFS in the ibrutinib arm was not reached because progression events occurred more slowly than in the ofatumumab arm. The PFS results represent a 79 percent reduction in the risk of progression or death in patients treated with ibrutinib compared to ofatumumab. PFS in the ofatumumab arm was 8.1 months (HR 0.215, 95% CI, 0.146 to 0.317; $P<0.0001$).

The OS median was also not reached in either arm because progression events occurred slowly. The OS results represent a 57 percent reduction in the risk of death in patients receiving ibrutinib versus those in the ofatumumab arm. The median follow-up was 9.4 months.

Additionally, the ORR was significantly higher in patients taking ibrutinib monotherapy versus ofatumumab monotherapy, regardless of response criteria or baseline characteristics. Overall, 43 percent of ibrutinib patients achieved a partial response (PR) compared to only four percent of patients taking ofatumumab ($p<0.0001$), following the International Workshop on CLL (IWCLL) response criteria requiring response to be confirmed for at least two months.

An additional 20 percent of ibrutinib treated patients also achieved a PR with lymphocytosis. Investigator-assessed response rates were 85 percent for ibrutinib and 24 percent for patients receiving ofatumumab. Significantly higher response rates were seen in the ibrutinib arm consistently across all baseline sub-groups, including those with a deletion of the short arm of chromosome 17, a genetic mutation typically associated with poor prognoses, or refractory to a purine analogue.

RESONATE is an international, open-label, randomized study that examined ibrutinib monotherapy versus ofatumumab monotherapy in relapsed or refractory patients with CLL/SLL who had received at least one prior therapy and were not considered appropriate candidates for treatment with a purine

analog (n=391). Patients were administered either 420 mg oral ibrutinib (n=195) once-daily until progression or unacceptable toxicity or intravenous ofatumumab for up to 24 weeks (n=196, initial dose of 300 mg followed by 11 doses at 2,000 mg, per dose and schedule consistent with local labeling).

Ibrutinib is a Bruton's tyrosine kinase inhibitor, and is marketed as Imbruvica in the U.S., where it received FDA approval for the treatment of patients with MCL who have received at least one prior therapy and for the treatment of patients with CLL who have received at least one prior therapy.

In 2011, Janssen and Pharmacyclics Inc. entered into an agreement to jointly develop and commercialize ibrutinib.

Prostate Cancer

Enzalutamide Extends PFS In Patients Not Treated With Chemotherapy

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The oral medication, which is marketed under the brand name Xtandi, also helped prevent bone metastases, delayed the need for chemotherapy, and reduced evidence of prostate cancer in the bloodstream.

"Based on the study results, this drug could fill an important gap in prostate cancer treatment today," said Tomasz Beer, the lead author on the study and deputy director of the Knight Cancer Institute at Oregon Health & Science University. "The strong response to this new use of enzalutamide shows that it can provide a viable, less toxic alternative to chemotherapy in staving off the disease in men who aren't responding to standard first line hormonal treatments."

Beer also holds the Grover C. Bagby Endowed Chair for Prostate Cancer Research, and in 2012 was selected as one of six scientists to take part in a Stand Up To Cancer Dream Team to study advanced prostate cancer.

The double-blind phase III study included 1,717 research participants enrolled at 207 sites globally between September 2010 and September 2012; 872 received enzalutamide while the others received a placebo. All patients enrolled had metastatic prostate cancer that was progressing despite treatment with traditional hormone therapy. None had yet received chemotherapy.

The trial, named PREVAIL, was concluded early following a planned interim analysis, due to treatment response. At this point, 72 percent of enzalutamide patients and 63 percent of placebo patients were alive at the trial cutoff date showing a 29 percent overall improvement in survival. Fatigue and hypertension were among the most common clinically relevant side effects.

Enzalutamide is approved by FDA for men whose disease has not been stopped by other treatments including surgery, radiation, androgen deprivation therapy and chemotherapy.

The drug's sponsors, Astellas Pharma Global Development and Medivation Inc., are collaborating on a comprehensive global development program that includes studies of enzalutamide across the full spectrum of advanced prostate cancer as well as advanced breast cancer. The companies jointly commercialize Xtandi capsules in the U.S. and Astellas is responsible for all global manufacturing and regulatory filings. During the study, Beer received grants from Astellas Pharma Global and Medivation.

Multiple Myeloma

Phase III PANORAMA-1 Trial Meets PFS Primary Endpoint

A phase III trial demonstrated a 37 percent improvement in progression-free survival when using the investigational compound LBH589 (panobinostat) in combination with bortezomib and dexamethasone compared to treatment with the same regimen with placebo in patients with relapsed or relapsed and refractory multiple myeloma.

The trial, PANORAMA-1, met its primary endpoint (HR=0.63 [95% CI: 0.52 to 0.76]; $p<0.0001$). The results were presented at the annual meeting of the American Society of Clinical Oncology in Chicago.

In the LBH589 arm, there was a 4-month prolongation of median PFS: 12 months compared to 8 months in the placebo arm. The effect of LBH589 was observed across all patient subgroups.

The findings also showed that adding LBH589 to bortezomib and dexamethasone led to a significant increase in higher quality responses compared to standard-of-care therapy alone, as evidenced by a nearly two-fold increase in complete/near complete response rates: 28 percent compared to 16 percent, respectively ($p=0.00006$).

PANORAMA-1 is a randomized, double-blind, global registration trial to evaluate LBH589 in combination with bortezomib and dexamethasone against bortezomib and dexamethasone alone in patients with relapsed or relapsed and refractory multiple myeloma who failed on at least one prior

treatment. The study of 768 patients took place in 215 clinical trial sites worldwide. Data for overall survival, a secondary endpoint, are not yet mature. Other secondary endpoints include overall response rate, duration of response and safety.

LBH589, a pan-deacetylase inhibitor, potentially provides a novel mechanism of action to treat multiple myeloma and works by blocking a key class of cancer cell enzymes, which ultimately leads to cellular stress and death of these cells.

In May, LBH589 was granted priority review by FDA and additional global regulatory submissions are underway, according to the drug's sponsor, Novartis.

Pancreatic Cancer

Vaccine, LDCT Pretreatment Primes PDACs for Immunotherapy

(Continued from page 1)

"Our study shows for the first time that treatment with a vaccine-based therapy directly reprograms the pancreatic cancer microenvironment, allowing the formation of lymphoid aggregates, which are organized, lymph node-like, functional immune structures, and which convert an immunologically quiescent tumor into an immunologically active tumor," said Lei Zheng, assistant professor of oncology and surgery at the Sidney Kimmel Comprehensive Cancer Center and the Skip Viragh Center for Pancreatic Cancer Research and Clinical Care at the Johns Hopkins University School of Medicine.

Researchers enrolled 59 patients between 2008 and 2012 and randomized them among three arms: patients in arm A received GVAX alone, patients in arm B received GVAX plus a single intravenous dose of cyclophosphamide at 200 mg/m2, and patients in arm C received GVAX plus 100 mg oral doses of cyclophosphamide once daily, on alternate weeks.

About two weeks after vaccination, all patients underwent surgery to remove their pancreatic tumors. Of the 59 patients, 39 remained grossly free of disease after surgery and underwent further treatment with chemotherapy and radiotherapy, and their tumors were analyzed in this study.

In addition to tumor samples from the 39 patients, the researchers used, for the comparative analyses, tumor samples from 58 patients from other studies: Four were unvaccinated patients and 54 were patients whose tumor samples were collected prior to vaccination. They found that the vaccine-chemotherapy combination resulted in the formation of lymphoid aggregates within the tumors in 33 of the 39 patients within two weeks of vaccination.

Extensive analysis of the various immune cell types found in the tumors after vaccination revealed an increase in the ratio of effector T cells to regulatory T cells. According to researchers, this meant that the tumors had become immunogenic and the immune cells in the tumor area were capable of fighting the cancer cells. An increase in the ratio was associated with better survival.

The researchers also found that the tumors from patients who survived for more than three years after vaccine therapy had enhanced signaling pathways that promote immune responses, compared with those who survived for less than 1.5 years following vaccination.

"We are further dissecting the immune signatures within the lymphoid aggregates to study the TGF-beta and Th17 signaling pathways. TGF-beta and Th17 pathways may also be key targets, in addition to PD-1/PD-L1, for treatments that enhance vaccine-induced antitumor immune responses in pancreatic cancer," said Zheng.

Thyroid Cancer

Phase III Trial Data: Lenvatinib Extends PFS by Over 14 Months

In a phase III trial of patients with progressive radioiodine-refractory differentiated thyroid cancer, lenvatinib significantly extended progression-free survival compared to placebo.

The median PFS with lenvatinib and placebo were 18.3 months and 3.6 months, respectively (HR=0.21, [99% CI, 0.14-0.31]; $p<0.0001$). The benefit was confirmed in all predefined subgroups of the study.

The study, named SELECT, was presented at the annual meeting of the American Society of Clinical Oncology in a Head and Neck Cancer oral session June 2.

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 involved in tumor proliferation.

SELECT was a multicenter, randomized, double-blind study to compare the PFS of patients with RR-DTC and radiographic evidence of disease progression within the prior 13 months, treated with once-daily,

oral lenvatinib versus placebo. The study enrolled 392 patients in over 100 sites in Europe, North and South America and Asia.

PFS was the primary endpoint for this study, and secondary endpoints included overall survival, overall response rate and safety. Median OS has not yet been reached.

Rates of complete response were 1.5 percent (4 patients) for the lenvatinib group and zero in the placebo group. The results for partial response were 63.2 percent (165 patients) in the lenvatinib group and 1.5 percent (2 patients) in the placebo arm. The median exposure duration was 13.8 months for lenvatinib and 3.9 months for placebo, and the median time to response for lenvatinib was 2.0 months.

Lenvatinib, sponsored by Eisai, was granted orphan drug designation for the treatment of follicular and papillary thyroid cancer by the European Commission in April 2013. FDA granted orphan status for follicular, medullary, anaplastic and metastatic or locally advanced papillary thyroid cancer.

Glioblastoma

Vaccine Increases PFS by 4 Months In Phase II Per-Protocol Analysis

A dendritic cell-based immunotherapeutic vaccine increased median overall survival by about four months in a phase II placebo-controlled study in newly diagnosed glioblastoma multiforme.

When overall survival and progression-free survival were assessed in pre-specified patient subgroups, results favored treatment with the ICT-107 vaccine over control in HLA-A2 patients within each of the two major MGMT subgroups (unmethylated and methylated).

While the subgroups were small in size, and not powered to show statistical significance, the numeric advantages in favor of ICT-107 treated patients were shown to be large and clinically meaningful, according to the drug's sponsor, ImmunoCellular Therapeutics Ltd.

The trial is a randomized, double-blind study of the safety and efficacy of ICT-107 in newly diagnosed patients with glioblastoma multiforme following resection and chemoradiation. ICT-107 is an intradermally administered autologous vaccine consisting of the patient's dendritic cells pulsed with six synthetic tumor-associated antigens: AIM-2, MAGE-1, TRP-2, gp100, HER-2, IL-13R 2. The control consists of the patient's unpulsed dendritic cells. The study was presented at the annual meeting of the American Society for Clinical Oncology in Chicago.

A total of 124 patients were randomized at 25 clinical trial sites in the U.S. All patients in the trial received standard-of-care temozolomide. The regimen is four induction doses of ICT-107 after chemoradiation, and then maintenance doses until the patient progresses.

The primary endpoint of the trial is OS. Other secondary endpoints include the rates of OS and PFS at six months after surgery, then assessed every three months until the end of the study. Safety and immune response are additional secondary endpoints. The subgroups analyzed in the phase II trial were based on age, gender, HLA type, MGMT status, performance status and resection status.

In the per-protocol analysis of data from HLA-A2 patients with unmethylated MGMT, the control and treated median OS times were 11.8 and 15.8 months, respectively, indicating about a 33 percent numeric survival increase for treated patients (HR=0.612, log-rank p-value=0.175).

The median PFS times for control and treated patients were 6.0 and 10.5 months, respectively, indicating about a 4.5-month or 75 percent numeric PFS increase for treated patients (HR=0.758, log-rank p-value=0.442).

In the per-protocol analysis of data from HLA-A2 patients with methylated MGMT, the control and treated groups had still not reached median survival times as of the time of data analysis, with the majority of patients still alive (65 percent of treated compared to 57 percent of control patients). However, the median PFS times for control and treated patients were 8.5 and 24.1 months, respectively, indicating about a 15.6-month or 184 percent statistically significant PFS increase for treated patients (HR=0.259, log-rank p-value=0.005).

ImmunoCellular is in the process of finalizing the design of the phase III protocol, in anticipation of discussions with the FDA and the European Medicines Agency. Plans are underway to request an end-of-phase II meeting with the FDA, anticipated to take place during the summer, according to the sponsor.

NCI CTEP-Approved Trials For the Month of June

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

9534: A Phase I Trial of Ibrutinib Plus PD 0332991 (Palbociclib) in Patients with Previously Treated Mantle Cell Lymphoma. Weill Medical College of Cornell University; Martin, Peter. (646) 962-2064

9540: A Phase 1 Study of Lenalidomide and Ibrutinib in Combination with Rituximab in Relapsed and Refractory CLL and SLL. MedStar Georgetown University Hospital; Ujjani, Chaitra S. (202) 444-1212

9552: A Phase 1 Study of MLN0128 and Bevacizumab in Patients with Recurrent Glioblastoma and Other Solid Tumors. Dana-Farber Cancer Institute; Nayak, Lakshmi. (617) 632-2166

9557: Phase I Study of AT13387 in Combination with Dabrafenib and Trametinib in BRAF-Inhibitor Resistant Patients with BRAF-Mutant Melanoma. Dana-Farber Cancer Institute; Sullivan, Ryan Joseph. (617) 724-4000

9585: Phase I Study of MLN0128 (NSC# 768435) in Combination with Ziv-Aflibercept (NSC# 724770) in Patients with Advanced Cancers. MD Anderson Cancer Center; Naing, Aung. (713) 563-0181

9762: Phase I Trial of the Combination of Bortezomib and Clofarabine in Adults with Refractory Solid Tumors. National Cancer Institute Developmental Therapeutics Clinic; Kummar, Shivaani. (301) 435-0517

AMC-090: A Phase 1/Pharmacokinetic Study of Erlotinib for Advanced Non-Small Cell Lung Cancer in Persons with HIV Infection. AIDS-Associated Malignancies Clinical Trials Consortium; Haigentz, Missak. (718) 920-4826

NRG-BR001: A Phase 1 Study of Stereotactic Body Radiotherapy (SBRT) for the Treatment of Multiple Metastases. NRG Oncology; Chmura, Steven J. (773) 702-7319

Phase II

9446: A Phase 2 Study of Trametinib in Combination with Radioiodine (RAI) for RAS Mutant or RAS/RAF Wild-Type, RAI-Refractory Recurrent and/or Metastatic Thyroid Cancers. Memorial Sloan Kettering Cancer Center; Ho, Alan Loh. (646) 888-4235

A091305: A Phase 2 Randomized Study of Efatutazone, an Oral PPAR Agonist, In Combination with Paclitaxel Versus Paclitaxel in Patients with Advanced Anaplastic Thyroid Cancer. Alliance for Clinical Trials in Oncology; Smallridge, Robert C. (904) 953-2392

Other Phases

A151221: Serum Androgens as Prognostic of Survival in Metastatic Castration Resistant Prostate Cancer. Alliance for Clinical Trials in Oncology; Ryan, Charles James. (415) 514-6380

AALL14B6-Q: Molecular Profiling to Impact the Management of Pre-B ALL: A Pilot Study. Children's Oncology Group; McGowan-Jordan, Jean. (613) 737-7600 X 2276

ANBL14B1-Q: Assessment of Fucsosyl-GM1 in High Risk Pediatric Neuroblastoma. Children's Oncology Group; Maris, John M. (215) 590-5244

EL613T1: Significance of IFN-alpha Adjuvant Therapy Treatment and Clinical Outcomes on BRAF V600E Mutation Vs. Wild Type Melanoma Patients in Correlation with Immunoscore Assessment. ECOG-ACRIN Cancer Research Group; Kirkwood, John Munn. (412) 623-7707

NRG-GU-TS001: Evaluation of MRE11 as a Biomarker in Muscle Invasive Bladder Cancer Treated with Chemoradiotherapy: A Secondary Analysis of RTOG 8802, 8903, 9506, and 9706, 9906 and 0233. NRG Oncology; Shipley, William U. (617) 726-8146

S9031-S9333-S0106-S0112-B: Identification and Development of Biomarkers Profiles to Predict Clinical Outcomes for Acute Myeloid Leukemia (AML) Patients with NPM1 pos/FLT3-ITD neg Genotype. SWOG; Stirewalt, Derek Lynn. (206) 667-5386

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FDA Approvals

Lymphoseek Label Updated To Include Head and Neck SCC

FDA approved a new use for Lymphoseek (technetium 99m tilmanocept) Injection, a radioactive diagnostic imaging agent, to determine the extent squamous cell carcinoma has spread in the body's head and neck region.

In 2013, Lymphoseek was approved to help identify lymph nodes closest to a primary tumor in patients with breast cancer or melanoma. It can now be used to guide testing of lymph nodes closest to a primary tumor for cancer, in patients with cancer of the head and neck.

Lymphoseek's safety and effectiveness were established in a clinical trial of 85 patients with squamous cell carcinoma of the lip, oral cavity, and skin. All patients were injected with Lymphoseek. Surgeons subsequently removed suspected lymph nodes—those identified by Lymphoseek and those based upon tumor location and surgical practice—for pathologic examination. Results showed that Lymphoseek–guided sentinel lymph node biopsy accurately determined if the cancer had spread through the lymphatic system.

Lymphoseek is marketed by Navidea Biopharmaceuticals Inc.

FDA approved Aloxi (palonosetron HCl) injection for the prevention of nausea and vomiting due to chemotherapy in children as young as one month to less than 17 years old, including highly emetogenic cancer chemotherapy.

This is the first approval of a product for acute chemotherapy-induced nausea and vomiting prevention in patients aged one month to six months.

The approval was based on a randomized, double-blind, non-inferiority pivotal trial comparing single-dose intravenous Aloxi 20 mcg/kg given 30 minutes prior to chemotherapy to a standard of care IV ondansetron regimen of 0.15 mg/kg given 30 minutes prior to chemotherapy followed by infusions four and eight hours after the first dose of ondansetron.

Within the first 24 hours after chemotherapy, complete response, defined as no vomiting, no retching and no antiemesis rescue medication, was achieved in 59.4 percent of patients who received Aloxi 20 mcg/kg versus 58.6 percent of those who received the ondansetron regimen, meet its primary endpoint.

Treatment-emergent adverse events were comparable across both arms, with the most frequently reported in the palonosetron group being headaches. While this study demonstrated that pediatric patients require a higher palonosetron dose than adults to prevent CINV, the safety profile was consistent with the established profile in adults. Aloxi is sponsored by Eisai Inc. and Helsinn Group.

FDA granted Orphan Drug Designation to mocetinostat, as a treatment for myelodysplastic syndrome, developed by Mirati Therapeutics Inc.

Mocetinostat is being evaluated in phase II clinical studies in combination with Vidaza as a treatment for intermediate and high-risk MDS, as well as a single agent treatment in patients with diffuse large B-cell lymphoma and bladder cancer targeting specific genetic mutations in histone acetylation that increase the likelihood of response in tumor cells.

The FDA's Office of Orphan Drug Products grants orphan status to support development of medicines for underserved patient populations or rare disorders that affect fewer than 200,000 people in theU.S.

Mocetinostat is an oral, spectrum-selective HDAC inhibitor. Thirteen clinical trials have been completed, which enrolled over 400 patients with a variety of hematologic malignancies and solid tumors. Mirati also plans to initiate phase II studies of mocetinostat as a single agent in patients with mutations in histone acetyl transferases in bladder cancer and DLBCL.

FDA approved the Invenia ABUS breast imaging technology, which uses 3D ultrasound to image women with dense breast tissue in approximately 15 minutes with new features that conform to the patient's body and provide enhanced images.

Its sponsor, GE Healthcare, says the system can help clinicians find 35.7 percent more cancers in women with dense breasts than mammograms alone.

The Invenia ABUS uses the Reverse Curve transducer to conform to a woman's anatomy, for better comfort and image performance. Further, the system uses Compression Assist, a feature which applies light levels of compression automatically to the breast for increased ease and image reproducibility.

The system will first be launched in Fairfax, Va., and Westchester County, N.Y., before being available nationwide later this year, according to GE Healthcare.