The Clinical Cancer Letter

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Leukemia

High-Risk Subset of CLL Patients Shows Benefit in Phase II Trial

A statistically significant percentage of chronic lymphocytic leukemia patients in a phase II clinical trial responded to venetoclax therapy.

The open-label study, sponsored by AbbVie, met its primary endpoint, achieving overall response rates in patients with relapsed/refractory or previously untreated CLL with 17p deletion, according to an independent review analysis.

The study enrolled 157 patients, 107 in the main study cohort evaluating efficacy, and 50 patients in the safety expansion cohort.

The primary efficacy endpoint is overall response rate, and the primary safety endpoints are the number and percentage of patients who experienced treatment-related adverse events, changes in physical exam findings, including vital signs, changes in clinical laboratory test results and changes in cardiac assessment findings.

(Continued to page 2)

Lung Cancer

Atezolizumab Immunotherapy Meets Response Endpoint in Phase II NSCLC Study

A phase II study of atezolizumab immunotherapy met its primary endpoint, shrinking tumors in patients with locally advanced or metastatic non-small cell lung cancer whose disease expressed PD-L1.

The study showed the amount of PD-L1 expressed by a person's cancer correlated with their response to the medicine.

The study, BIRCH, is an open-label, multicenter, single-arm study that evaluated the safety and efficacy of atezolizumab in 667 people. Results from the study will be presented at an upcoming medical meeting, according to the drug's sponsor, Genentech, a member of the Roche Group.

(Continued to page 3)

Drugs and Targets

European Commission Approves Unituxin In Pediatric High-Risk Neuroblastoma

The European Commission granted a marketing authorization for Unituxin (dinutuximab) for the treatment of high-risk neuroblastoma in patients aged 12 months to 17 years, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and autologous stem cell transplantation.

Unituxin is administered in combination with granulocyte-macrophage colony-stimulating factor, interleukin-2, and isotretinoin.

The European approval was based on demonstration of improved

(Continued to page 6)

Deletion 17p CLL Patients Show Benefit in Venetoclax Trial

(Continued from page 1)

Secondary efficacy outcome measures include complete remission rate, partial remission rate, duration of response, overall survival and progression-free survival, among others.

"The results from this study demonstrate the clinical activity of venetoclax in patients with relapsed/refractory CLL who have 17p deletion, a patient population that has historically been difficult to treat," said Michael Severino, executive vice president of research and development and chief scientific officer at AbbVie.

Venetoclax is an inhibitor of the B-cell lymphoma-2 protein. The BCL-2 protein prevents apoptosis of some cells, including lymphocytes, and can be expressed in some cancer types.

Data from this study will be presented at an upcoming medical conference and will serve as the pivotal registration data for applications to the FDA, EMA and other health authorities, according to the drug's sponsor.

The safety profile was similar to previous studies and no unexpected safety signals were reported for venetoclax.

Venetoclax is being developed in partnership with Genentech and Roche, and was formerly known as ABT-199.

In 2015, the FDA granted Breakthrough Therapy Designation to venetoclax for the evaluation of treatment of CLL in previously treated (relapsed/refractory) patients with the 17p deletion genetic mutation. Phase I, II and III clinical trials for venetoclax are ongoing, both as a monotherapy and in combination with other therapies.

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Liver Cancer

ThermoDox plus RFA Increase OS By 58 Percent in HEAT Study

The latest overall survival analysis of the HEAT Study, which is evaluating ThermoDox and radiofrequency ablation in hepatocellular carcinoma, showed that a subgroup of patients demonstrated an average 58 percent improvement in overall survival.

Median overall survival for the ThermoDox (heat-activated, liposomal-encapsulated doxorubicin) arm was 79 months, compared to 53.6 months in patients receiving optimized RFA alone (HR=0.63 [95% CI 0.43-0.93]; p=0.0198).

In the most recent post-hoc analysis of the HEAT Study, data continued to support ThermoDox's potential to significantly improve OS compared to an RFA control in patients with lesions that undergo optimized RFA treatment for 45 minutes or more, according to the drug's sponsor, Celsion Corp.

Findings from this analysis apply to patients with single HCC lesions (64.4 percent of the HEAT Study population [n=701]) from both size cohorts of the HEAT Study (3-5 cm and 5-7 cm), representing a subgroup of 285 patients.

Additional findings from this most recent analysis specific to the Chinese cohort of patients with single lesions (74 percent of the HEAT Study Chinese patient population) showed a 75 percent improvement (HR=0.57; p=0.08) in OS for the ThermoDox plus optimized RFA group compared to optimized RFA only group.

Patients in the Chinese cohort with single lesions between 3-5 cm showed a doubling of improvement (HR=0.50; p=0.06) in OS when treated with ThermoDox plus optimized RFA.

"The continuing strength of the HEAT Study data reinforces our confidence in ThermoDox® as the first and only front line therapy for newly diagnosed HCC patients and further improves the risk profile of our Phase III OPTIMA Study, currently enrolling patients in 12 countries globally," said Michael Tardugno, Celsion's chairman, president and CEO.

"Equally important is the maturing data and the remarkable clinical benefit seen in the Chinese patient cohort. This large 221 patient subgroup represents a country with over 50 percent of the world's incidence (over 400,000 new cases) of HCC every year. These specific findings, along with the 25.4 months improvement in time to death seen in the global population, strengthen our options for discussions with the CFDA to identify a faster path to commercialization."

The OPTIMA Study is expected to enroll up to 550 patients in up to 75 clinical sites in the United States, Europe, China and Asia Pacific, and will evaluate ThermoDox in combination with optimized RFA, which will be standardized to a minimum of 45 minutes across all investigators and clinical sites for treating lesions three to seven centimeters, versus standardized RFA alone. The primary endpoint for the trial will be overall survival.

Lung Cancer

Atezolizumab Shows Response In Phase II NSCLC Study

(Continued from page 1)

People in the study received a 1200-milligram intravenous dose of atezolizumab every three weeks. The primary endpoint of the study was objective response rate. Secondary endpoints included duration of response, overall survival, progression-free survival and safety. Adverse events were consistent with what has been previously observed for atezolizumab.

PD-L1 expression was assessed on both tumor cells and tumor-infiltrating immune cells with an investigational immunohistochemistry test being developed by Roche Diagnostics. Eligibility criteria included people whose tumors were determined to express PD-L1 with an IHC score of TC2/3 or IC2/3.

Atezolizumab (MPDL3280A) is an investigational monoclonal antibody designed to target PD-L1 expressed on tumor cells and tumor-infiltrating immune cells, preventing it from binding to PD-1 and B7.1 on the surface of T cells. By inhibiting PD-L1, atezolizumab may enable the activation of T cells, according to Genentech.

All studies of atezolizumab include the evaluation of an investigational IHC test that uses the antibody SP142 to measure PD-L1 expression on both tumor cells and infiltrating immune cells. There are 11 ongoing or planned phase III studies of atezolizumab across certain kinds of lung, kidney, breast and bladder cancer.

"We are encouraged by the number of people who responded to atezolizumab and maintained their response during the study, which is particularly meaningful for people who had received several prior treatments," said Sandra Horning, chief medical officer and head of Global Product Development at Genentech.

"We plan to present results at an upcoming medical meeting and will discuss these data as well as results from our other lung cancer studies with health authorities to bring this medicine to patients as quickly as possible."

Earlier this year, the FDA granted atezolizumab a Breakthrough Therapy Designation for the treatment of people whose NSCLC expresses PD-L1 and who progressed during or after standard treatments.

Study: SBRT Effective Treatment In Tumors Larger Than 5 cm

Non-invasive stereotactic body radiation therapy is effective and well-tolerated by patients with inoperable non-small cell lung cancer tumors that are larger than 5 cm but had not spread from the lung to the lymph nodes or outside of the chest—i.e.: early stage, or node negative—according to a retrospective study published in the International Journal of Radiation Oncology Biology Physics.

The study involved the use of SBRT for the treatment of frail patients with large inoperable lung tumors and without lymph node involvement. SBRT has not typically been used to treat large tumors.

Results from SBRT were compared with literature on outcomes from conventional lung surgery. The research suggests that non-invasive SBRT may be a viable treatment alternative to conventional surgery for some patients with larger lung tumors.

"Our study shows that lung SBRT can be used to safely treat localized node-negative inoperable NSCLC tumors larger than 5 cm, with low rates of recurrence at the primary tumor site and with minimal side effects," said Gregory Videtic, from the Department of Radiation Oncology at the Cleveland Clinic Taussig Cancer Institute, and professor of medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University.

Prior to the emergence of lung SBRT, frail medically compromised patients with node-negative inoperable NSCLC were often treated with external beam radiation therapy which delivers lower doses over a higher number of treatment sessions. However, these patients often experienced a high rate of disease recurrence along with significant side effects.

Lung SBRT has become routine for treating small

NSCLC tumors, typically less than 3 cm, because of its high rate of local control and limited toxicity.

In their retrospective study, the researchers evaluated the outcomes of 40 patients with node-negative medically inoperable NSCLC whose primary tumors were greater than 5 cm and who were treated with SBRT between December 2003 and June 2014.

The study reviewed patients' outcomes at 18 months after treatment. Local control was achieved in 91.2 percent of the cases. The percentage of patients who experienced distant failure where cancer had spread to other parts of the body was 32.5 percent. When these results were compared to published surgical studies, lung SBRT appeared to have similar rates of local control and similar rates of distant failure.

Disease-free survival in patients who had no lung cancer present at 18 months after treatment was 34.6 percent. The overall survival rate at 18 months, including disease-free patients and those who still had evidence of lung cancer, was 59.7 percent.

"The overall survival rates are lower in medically inoperable patients receiving lung SBRT compared to operable surgical patients," said Videtic.

"However, the lower survival rate in medically inoperable patients may be due to the presence of other non-cancer related conditions, such as chronic obstructive pulmonary disease, commonly found in inoperable patients."

The percentage of SBRT patients who were free of side effects was 70.5 percent. Side effects observed from SBRT included mild chest wall pain and modest inflammation in lung tissue. In two severe cases, patients experienced excessive fluid build-up in the lung and a lung collapse due to inflammation that blocked the airways.

Carcinoid Syndrome

Oral Telotristat Etiprate Trial Meets Phase III Primary Endpoint

The TELESTAR trial demonstrated significant benefits in evaluating oral telotristat etiprate in the treatment of cancer patients with carcinoid syndrome, and met its primary endpoint.

Top-line results from the phase III trial showed that patients who added telotristat etiprate to the standard of care at both the 250 mg and 500 mg doses experienced a statistically significant reduction from baseline compared to placebo in the average number of daily bowel movements over the 12-week study period ($p<0.001$).

If approved, telotristat etiprate would be the first oral treatment successfully developed for carcinoid syndrome and the first addition to the standard of care in more than 16 years, according to the drug's sponsor, Lexicon Pharmaceuticals Inc. The current standard of care for carcinoid syndrome is somatostatin analog depot injection, first approved in 1998.

"Carcinoid syndrome is severely debilitating, preventing many patients from leading active and predictable lives, and unfortunately, a majority of patients will not be adequately controlled over time with the current standard of care," said Lonnel Coats, Lexicon president and CEO. "We are committed to working closely with the FDA to file our first new drug application and to bring this innovative new treatment to patients whose lives are already impacted by the challenges of cancer."

Lexicon received Fast Track designation and Orphan Drug status for telotristat etiprate from FDA in 2008 and 2012, respectively. The company plans to announce complete results from the Phase 3 TELESTAR study at an upcoming scientific conference.

NCI CTEP-Approved Trials For the Month of August

The National Cancer Institute Cancer Therapy Evaluation Program approved the following clinical research studies last month. For further information, contact the principal investigator listed.

Phase I

9782: A Phase 1 Study of BMN 673 in Combination with Carboplatin and Paclitaxel in Patients with Advanced Solid Tumors. Rutgers University - Cancer Institute of New Jersey LAO; Wisinski, Kari Braun. (608) 263-6222

9824: A Phase 1 Study of Alisertib (MLN8237) in Combination with mFOLFOX in Gastrointestinal Tumors. Yale University Cancer Center LAO; Goff, Laura Williams. (615) 322-4967

9853: A Phase 1 Study of AZD1775 in Combination with Belinostat in Relapsed and Refractory Myeloid Malignancies and Selected Untreated Patients with Acute Myeloid Leukemia. Moffitt Cancer Center P2C; Shafer, Danielle Aimee. (804) 628-0279

Phase II

9742: Multicenter Phase II Study of Nivolumab in Previously Treated Patients with Recurrent and Metastatic Nasopharyngeal Carcinoma. Mayo Clinic Cancer Center P2C; Ma, Brigette Buig-Yue. 852-26322118

A091401: Randomized Phase II Study of Nivolumab with or Without Ipilimumab in Patients with Metastatic or Unresectable Sarcoma. Alliance for Clinical Trials in Oncology; D'Angelo, Sandra Pierina. (646) 888-4159

Phase III

A061402: Solitary Plasmacytoma of Bone: Randomized Phase III Trial to Evaluate Treatment with Adjuvant Systemic Treatment and Zoledronic Acid Versus Zoledronic Acid After Definite Radiation Therapy. Alliance for Clinical Trials in Oncology; Mahindra, Anuj Kumar. (415) 476-9492

S1404: A Phase III Randomized Trial Comparing High Dose Interferon to MK-3475 (Pembrolizumab) in Patients with High Risk Resected Melanoma. SWOG; Grossmann, Kenneth F. (801) 587-4289

URCC-14040: A Randomized Clinical Trial Comparing the Effectiveness of Yoga, Survivorship Health Education, and Cognitive Behavioral Therapy for Treating Insomnia in Cancer Survivors. University of Rochester NCORP Research Base; Mustian, Karen M. (585) 275-5513

Other Phases

A151432: Homologous Recombination Deficiency Biomarker to Predict pCR with Platinum-Based Therapy in Patients with Triple Negative Breast Cancer Treated on CALGB 40603. Alliance for Clinical Trials in Oncology; Carey, Lisa A. (919) 966-4431

A221405: A Study Evaluating the Pregnancy Outcomes and Safety of Interrupting Endocrine Therapy for Young Women with Endocrine Responsive Breast Cancer who Desire Pregnancy. Alliance for Clinical Trials in Oncology; Partridge, Ann Hart. 617-632-2335

ABTR14B3-Q: Immunogenomics to Create New Therapies for High-Risk Childhood Cancers. Children's Oncology Group; Sorensen, Poul Henrik Bredahl. (604) 875-2936

AEWS15B4-Q: Evaluation of ctDNA as a Diagnostic and Prognostic Tool in Ewing Sarcoma. Children's Oncology Group; DuBois, Steven G. (415) 476-4764

ANBL14B7-Q: Preliminary Studies of Circulating GD2 as a Predictive Biomarker in Neuroblastoma NBL. Children's Oncology Group; Desai, Ami V. (267) 207-5032

ANBL15B1-Q: EphB4 and EphrinB2 as Therapeutic Targets in Neuroblastoma. Children's Oncology Group; Keller, Charles. (503) 494-1210

C10403T1: Correlation of Minimal Residual Disease (MRD) with Treatment Outcomes in Adolescents and Young Adults with Acute Lymphoblastic Leukemia : Results of US Intergoup Trial C-10403. ECOG-ACRIN Cancer Research Group; Stock, Wendy. (773) 834-8982

CLC.2E: A Prospective Economic Analysis of NCIC CTG CLC.2/Alliance A041202: A Randomized Phase III CLL Study of Bendamustine Plus Rituximab Versus Ibrutinib Plus Rituximab Versus Ibrutinib Alone in Untreated Older Patients (>= 65 Years of Age) with Chronic Lymphocytic Leukemia (CLL). NCIC Clinical Trials Group; Cheung, Matthew. (416) 480-4928

S0016C: Quantifying Genetic Diversity in Follicular Lymphoma to Predict Disease Progression. SWOG; Burack, W. Richard (585) 276-1885

Drugs and Targets

EC Approves Unituxin In Pediatric Neuroblastoma

(Continued from page 1)

event-free survival and overall survival in a multicenter, open-label, randomized trial (ANBL0032) sponsored by NCI under a Cooperative Research and Development Agreement with the drug's sponsor, United Therapeutics Corp., and conducted by the Children's Oncology Group.

The trial randomized (1:1) 226 patients to either the Unituxin/13-cis-retinoic acid arm or to RA alone. Patients in each arm received six cycles of treatment.

The Unituxin/RA arm consisted of Unituxin in combination with GM-CSF and RA (cycles 1, 3, and 5), Unituxin in combination with IL-2 and RA (cycles 2 and 4), and RA (cycle 6). Patients were 11 months to 15 years of age, with a median age 3.8 years.

The major efficacy outcome measure was investigator-assessed EFS, defined as the time from randomization to the first occurrence of relapse, progressive disease, secondary malignancy or death.

The primary intent-to-treat analysis found an improvement in EFS associated with Unituxin immunotherapy plus isotretinoin as compared to isotretinoin alone. The two-year estimates of EFS were 66 percent among subjects receiving Unituxin immunotherapy plus isotretinoin as compared with 48 percent in subjects receiving isotretinoin alone (log-rank test $p = 0.033$), although this difference did not reach formal statistical significance according to the pre-specified plan for interim analyses.

In addition, OS was evaluated with three years of follow-up after the EFS analysis as a secondary endpoint with a significant improvement observed among ITT subjects randomly allocated to receive Unituxin immunotherapy plus isotretinoin as compared with isotretinoin alone. The three-year estimates of OS were 80 percent compared with 67 percent among subjects receiving Unituxin immunotherapy plus isotretinoin and isotretinoin alone, respectively (log-rank test $p = 0.0165$).

Long-term overall survival was evaluated with five years of follow up after the EFS analysis and continued to demonstrate a survival advantage for patients who received Unituxin immunotherapy compared to those who received isotretinoin alone. The five-year estimates of OS were 74 percent for Unituxin immunotherapy compared to 57 percent for isotretinoin alone (log-rank test $p = 0.030$).

The most frequently occurring adverse reactions reported during the neuroblastoma studies were hypotension, pain, hypersensitivity, pyrexia, urticaria, capillary leak syndrome, anemia, hypokalemia, decreased platelet count, hyponatremia, increased alanine aminotransferase, decreased lymphocyte count and decreased neutrophil count. Additional adverse reactions characteristic of an allergic response were also reported, including anaphylactic reaction and bronchospasm.

Unituxin is a monoclonal chimeric antibody composed of murine variable heavy and light chain regions and the human constant region for the heavy chain kappa, and reacts specifically with the ganglioside GD2, which is highly expressed on the surface of the neuroblastoma cells and minimally expressed on the surface of normal human neurons, peripheral pain fibres, and skin melanocytes.

In March, Unituxin, in combination with GM-CSF, IL-2 and RA, became the first therapy to be approved by FDA for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multi-agent multimodality therapy.

Unituxin carries a Boxed Warning alerting patients and health care professionals that Unituxin irritates nerve cells, causing severe pain that requires treatment with intravenous narcotics and can also cause nerve damage and life-threatening infusion reactions, including upper airway swelling, difficulty breathing, and low blood pressure, during or shortly following completion of the infusion. Unituxin may also cause other serious side effects including infections, eye problems, electrolyte abnormalities and bone marrow suppression.

Health Canada issued a Notice of Compliance with Conditions for Imbruvica (ibrutinib) an oral, once-daily single-agent therapy for the treatment of patients with relapsed or refractory mantle cell lymphoma.

The approval with conditions is based on phase II clinical trial data that were published in the New England Journal of Medicine, showing an overall response rate of nearly 68 percent based on investigator assessment.

Imbruvica is co-developed by Cilag GmbH International, a member of the Janssen Pharmaceutical Companies, and Pharmacyclics LLC, an AbbVie company. Janssen Inc. markets Imbruvica in Canada.

Imbruvica was first approved in Canada in November 2014 for the treatment of patients with the

blood cancer chronic lymphocytic leukemia, including those with 17p deletion, who have received at least one prior therapy, or for the frontline treatment of patients with CLL with 17p deletion. For this clinical use, Imbruvica was issued marketing authorization without conditions.

FDA granted Orphan Drug Designation to Toca 511 & Toca FC, an investigational immunotherapy treatment for glioblastoma developed by Tocagen.

The agency recently granted the drug Fast Track designation for the treatment of recurrent high-grade glioma, which includes glioblastoma and anaplastic astrocytoma. According to Tocagen, the drug is planned to move into a clinical trial later this year.

Toca 511 & Toca FC is an investigational treatment that is designed to program cancer cells to convert the prodrug 5-FC into the anticancer drug 5-FU, killing tumor cells and leading to activation of the immune system via a combination of mechanisms.

Toca 511 is a retroviral replicating vector that selectively delivers a gene for the enzyme cytosine deaminase to the tumor. Patients then take oral cycles of Toca FC, a novel formulation of an antifungal drug, which is converted within infected cancer cells into the FDA-approved anticancer drug, 5-fluorouracil. Immune activation locally in the tumor occurs through a combination of mechanisms that together break the barrier of immune tolerance and may lead to durable tumor response, according to Tocagen.

FDA granted Orphan Drug Designation for MTG-201, a therapy targeting Dickkopf-3 gene defects in various cancers, for the treatment of malignant mesothelioma.

The Dickkopf-3 gene produces a protein called REIC (Reduced Expression in Immortalized Cells protein), which is a critical protein in the downstream mechanism of apoptosis and when absent cancer cells cannot die.

By expressing REIC protein from within cancer cells, MTG-201 induces selective apoptosis due to ER stress, directly killing the cancer and reducing cancer burden. MTG-201 also stimulates the production of activated T-cell lymphocytes that specifically target and destroy residual cancer cells.

MTG-201, developed by MTG Biotherapeutics, is currently in phase I clinical trials for the treatment of prostate cancer and mesothelioma. Preclinical programs are ongoing for the treatment of liver and bladder cancers. MTG-201 is also being evaluated for efficacy in combination with anti-PD-1, anti-PD-L1 and anti-CTLA-4 antibodies.

The European Commission, acting on the positive recommendation from the European Medicines Agency Committee for Orphan Medicinal Products, **granted orphan drug designation to synthetic hypericin,** the active pharmaceutical ingredient in SGX301, for the treatment of cutaneous T-cell lymphoma, a rare disease and a class of non-Hodgkin's lymphoma.

SGX301 has previously been granted both orphan drug and fast track designations from the FDA for the first-line treatment of CTCL.

Soligenix Inc., the drug's sponsor, is currently working with leading CTCL centers, as well as with the National Organization for Rare Disorders and the Cutaneous Lymphoma Foundation to begin a 120 subject pivotal phase III clinical trial with SGX301 in the second half of 2015.

SGX301 is a novel, first-in-class, photodynamic therapy utilizing visible light for activation. Synthetic hypericin is a potent photosensitizer which is topically applied to skin lesions and activated by visible fluorescent light.

In a phase II, double-blind, placebo-controlled clinical study in CTCL patients, the drug was safe and well tolerated, with 58.3 percent of the CTCL patients responding to SGX301 treatment compared to only 8.3 percent receiving placebo ($p <= 0.04$).

AstraZeneca and Heptares Therapeutics entered into a licensing agreement under which AstraZeneca will acquire exclusive global rights to develop, manufacture and commercialize the adenosine A2A receptor antagonist HTL-1071, a small molecule immuno-oncology candidate.

AstraZeneca will focus on exploring HTL-1071 and any additional compounds across a range of cancers, including in combination with its existing portfolio of immunotherapies.

The companies will also collaborate to discover further A2A receptor-blocking compounds for development in cancer immunotherapy.

Heptares will receive an upfront payment of $10 million and is eligible to receive additional milestone payments based on agreed pre-clinical and clinical events. Subject to successful completion of development and commercialization milestones, Heptares is also eligible to receive more than $500 million as well as royalty payments.

Mirati Therapeutics Inc. and MedImmune, the global biologics research and development arm of AstraZeneca, announced they have entered into an **exclusive clinical trial collaboration.**

The phase I/II study will evaluate the safety and efficacy of Mirati's investigational spectrum-selective histone deacetylase inhibitor, mocetinostat, in combination with MedImmune's investigational anti-PD-L1 immune checkpoint inhibitor, durvalumab (MEDI4736).

This novel combination will initially be evaluated in patients with non-small cell lung cancer with the potential to explore additional indications in the future.

Mocetinostat selectively inhibits class I HDAC enzymes, which has the potential to enhance the positive effect of checkpoint inhibitors, such as durvalumab, on tumor immunity, while durvalumab is designed to counter the tumor's immune-evading tactics by blocking a signal that helps tumors avoid detection.

Under the terms of the agreement, Mirati will conduct and fund the initial phase I/II clinical trial, which is expected to start in 2016, and MedImmune will supply durvalumab for the trial.

In the event that the initial clinical trial demonstrates positive results, MedImmune will have an exclusive period of time in which to negotiate a commercial license for the combination in this indication.

FDA and the European Medicines Agency have accepted regulatory applications for Gilotrif (afatinib), sponsored by Boehringer Ingelheim, for treatment of advanced squamous cell carcinoma of the lung, after treatment with first-line chemotherapy.

Gilotrif has also been granted Orphan Drug Designation by the FDA.

The submissions are based on positive data from the phase III LUX-Lung 8 study that showed a significant delay in progression of lung cancer and a significant improvement in overall survival for Gilotrif compared to Tarceva (erlotinib).

Data from LUX-Lung 8 showed that treatment with Gilotrif resulted in superior progression-free survival, reducing the risk of cancer progression by 19 percent, and superior overall survival, reducing the risk of death by 19 percent compared to Tarceva.

More patients had improved overall health-related quality-of-life with Gilotrif than with Tarceva (36 vs. 28 percent). Significantly more patients had an improvement in cough with Gilotrif than with Tarceva (43 vs. 35 percent).

Afatinib, an oral, once daily EGFR-directed therapy, is currently approved in more than 60 countries for the first-line treatment of specific types of EGFR mutation-positive NSCLC (under brand names Gilotrif and Giotrif). Approval of afatinib in this indication was based on the primary endpoint of PFS from the LUX-Lung 3 clinical trial where afatinib significantly delayed tumor growth when compared to standard chemotherapy.

In addition, afatinib is the first treatment to show an OS benefit for patients with specific types of EGFR mutation-positive NSCLC compared to chemotherapy. A significant OS benefit was demonstrated independently in the LUX-Lung 3 and 6 trials for patients with the most common EGFR mutation (exon 19 deletions) compared to chemotherapy.

ImmunoCellular Therapeutics Ltd. reached an agreement with the FDA on a Special Protocol Assessment for its phase III registrational trial of the cancer immunotherapy ICT-107 in newly diagnosed glioblastoma.

The trial is designed as a randomized, double-blind, placebo-controlled study of about 400 HLA-A2 positive patients, which will be conducted at about 120 sites in the U.S., Canada and the E.U.

The primary endpoint in the trial is overall survival. Secondary endpoints include progression-free survival and safety, as well as overall survival in the two pre-specified MGMT subgroups.

Andrew Gengos, ImmunoCellular's CEO, commented: "We are making significant progress toward establishing our clinical site network and obtaining the necessary institutional review board approvals. We are confident that we are on track to begin patient enrollment in the late third quarter or early fourth quarter of this year."

Gamida Cell reached agreements with the FDA and EMA regarding its phase III study design outline of NiCord. The company plans to commence an international, multi-center study of NiCord in 2016. Phase I/II data of 15 patients are expected in the fourth quarter of this year.

NiCord is in development as an experimental treatment for various types of blood cancers including AML, ALL, MDS and CML.

NiCord is derived from a single cord blood unit which has been expanded in culture and enriched with stem cells using Gamida Cell's NAM technology. It is intended as a treatment for blood cancer patients indicated for bone marrow transplantation who do not have a family related matched donor.

The phase III study will be a randomized, controlled study of around 120 patients. It will compare patients transplanted with NiCord to those transplanted with un-manipulated umbilical cord blood.