

The Clinical Cancer Letter

September 2014

• www.cancerletter.com

• Vol. 37 No. 9

Breast Cancer

Final Results from CLEOPATRA Phase III Trial Show Perjeta Increased OS 15.7 Months

Final phase III trial results showed that adding Perjeta to Herceptin and docetaxel chemotherapy increased overall survival to over four-and-a-half years in patients with previously untreated HER2-positive metastatic breast cancer.

Data from the CLEOPATRA study showed that the addition of Perjeta (pertuzumab) increased median overall survival 15.7 months compared to Herceptin (trastuzumab) and docetaxel alone—to 56.5 and 40.8 months, respectively.

The data were presented at the Presidential Symposium at the European Society for Medical Oncology Congress in Madrid.

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Pancreatic Neuroendocrine Tumors

Afinitor Increases Overall Survival To 3.5 Years in Phase III Trial

An analysis of mature overall survival data from a phase III trial showed that Afinitor increased median overall survival by 6.34 months compared to placebo, for a total of over 3.5 years in patients with well-differentiated advanced and progressive pancreatic neuroendocrine tumors.

Overall survival was a secondary endpoint of the trial. The findings were presented at the European Society for Medical Oncology Congress in Madrid. Results from the primary analysis, which focused on progression-free survival, in which Afinitor (everolimus) more than doubled median PFS compared to placebo, were previously published in the New England Journal of Medicine.

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Non-Small Cell Lung Cancer

Merck Serono Cancels Tecemotide Program In NSCLC, Including Two Phase III Trials

Merck Serono will discontinue its worldwide clinical development program of MUC1 antigen-specific immunotherapy tecemotide as a monotherapy in stage III non-small cell lung cancer. This includes the phase III START2 and INSPIRE studies.

The decision comes after a planned analysis of EMR 63325-009, a randomized, double-blind, placebo-controlled phase I/II study in Japanese patients with stage III unresectable, locally advanced NSCLC. Patients had received concurrent or sequential chemoradiotherapy with a minimum of two cycles of platinum-based chemotherapy and radiation dose greater than or equal to 50 Gy.

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Perjeta Addition Increases OS By 15.7 Months in Phase III Trial

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“Adding Perjeta to treatment with Herceptin and chemotherapy resulted in the longest survival observed to date in a clinical study of people with HER2-positive metastatic breast cancer,” said Sandra Horning, chief medical officer and head of Global Product Development at Genentech, Perjeta’s sponsor.

Perjeta in combination with Herceptin and docetaxel chemotherapy is approved in the U.S. and the European Union for people with previously untreated HER2-positive metastatic breast cancer.

CLEOPATRA was an international, randomized, double-blind, placebo-controlled study. The study evaluated 808 patients with previously untreated HER2-positive MBC, or with HER2-positive MBC that had come back after prior therapy in the adjuvant or neoadjuvant setting. The primary endpoint of the study was progression-free survival.

An interim OS analysis was previously presented at the San Antonio Breast Cancer Symposium in 2012. At the time of the analysis, median OS had not yet been reached for people receiving the Perjeta regimen as more than half of these people continued to survive.

The results presented at the ESMO Congress are from the final pre-specified OS analysis after a median follow-up of 50 months. No new safety signals were observed.

An updated analysis of previously reported

CLEOPATRA survival data showed that risk of death was reduced by 32 percent for people who received Perjeta, compared to those who received Herceptin and chemotherapy (HR=0.68, 95% CI 0.56-0.84; p=0.0002); those patients also had a 32 percent reduction in the risk of their disease worsening or death (HR=0.68, 95% CI 0.58-0.80).

With longer follow-up, the median PFS improvement of more than six months was maintained—median PFS of 18.7 months for patients in the Perjeta arm, compared to 12.4 months for those who received Herceptin and chemotherapy.

These data will be submitted to regulatory authorities around the world for inclusion in the prescribing information for Perjeta.

Perjeta is designed to prevent the HER2 receptor from pairing with other HER receptors on the surface of cells, a process that is believed to play a role in tumor growth and survival. Binding of Perjeta to HER2 may also signal the body’s immune system to destroy the cancer cells.

The mechanisms of action of Perjeta and Herceptin are believed to complement each other, as both bind to the HER2 receptor, but to different places. The combination of Perjeta and Herceptin is thought to provide a more comprehensive blockade of HER signaling pathways.

Multiple Myeloma Phase III Trial: Panobinostat Increases PFS by Four Months

Panobinostat demonstrated a four-month improvement in median progression-free survival in relapsed and/or refractory multiple myeloma, in combination with bortezomib and dexamethasone, in a phase III trial.

In the trial, named PANORAMA-1, the addition of panobinostat (LBH589) also led to clinically meaningful increases in complete and near complete response rates and duration of response, compared to bortezomib and dexamethasone plus placebo. The effect was observed across all patient subgroups.

According to Novartis, the drug’s sponsor, this is the first phase III study to demonstrate PFS superiority (HR=0.63 [95% CI: 0.52 to 0.76]; p<0.0001) of a three-drug over a two-drug combination in this patient population. Data was published in *The Lancet Oncology*. Overall survival data, the key secondary endpoint of the trial, are not yet mature.

THE CLINICAL CANCER LETTER

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PANORAMA-1 is a randomized, double-blind, placebo-controlled, multicenter global registration trial of 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.

If approved, panobinostat, a pan-deacetylase inhibitor, will be first in its class of anticancer agents available to this population. As an epigenetic regulator, panobinostat may help restore cell programming in multiple myeloma.

Side effects were consistent with those previously seen in LBH589 studies. The most common Grade 3/4 adverse events in the panobinostat combination arm were thrombocytopenia, lymphopenia, neutropenia, diarrhea and neuropathy. Adverse events were generally manageable through supportive care and dose reductions.

Based on the PANORAMA-1 data, panobinostat was granted priority review by FDA in May, and a regulatory application was submitted to the European Medicines Agency. Additional global regulatory submissions are underway, according to Novartis.

Pancreatic Neuroendocrine Tumors **Afinitor Increases Median OS** **To Over 3.5 Years in Phase III Trial**

(Continued from page 1)

Results from the trial, named RADIANT-3, showed a median OS of 44.02 months (95% CI: 35.61, 51.75) in patients treated with Afinitor plus best supportive care, and 37.68 months (95% CI: 29.14, 45.77) in the placebo arm.

The 6.34 month difference between the two arms was not statistically significant (HR 0.94; 95% CI: 0.73, 1.20; p=0.300). According to the drug's sponsor, Novartis, a high crossover of patients from placebo to Afinitor (85 percent) likely contributed to the long median OS in the placebo arm of 37.68 months, and may have confounded the ability to detect a difference in the OS results.

"The median overall survival of 44 months for everolimus is unprecedented in controlled clinical trials for advanced progressive pancreatic neuroendocrine tumors," said lead investigator James Yao, of MD Anderson Cancer Center. "The results affirm the importance of targeting key pathways involved in tumor growth, such as the mTOR pathway in advanced pNET."

RADIANT-3 is a prospective, double-blind, parallel group study. The core phase of the trial examined the efficacy and safety of Afinitor plus BSC

versus placebo plus BSC in 410 patients with advanced, low- or intermediate-grade pancreatic NET, also known as islet cell tumors.

Patients who met the study entry criteria were randomized 1:1 to receive either everolimus 10 mg once-daily (n=207) or daily placebo (n=203) orally, both in conjunction with BSC.

Patients on placebo whose disease progressed during the core phase were allowed to cross over to open-label Afinitor. In addition, when all patients were unblinded at the end of the core phase, those initially assigned to placebo were offered to switch to open-label Afinitor and those in the Afinitor arm could transition to open-label Afinitor.

During the open label phase patients continued with treatment until disease progression was documented by the investigator. At this point, patients discontinued the study drug and entered the follow-up period to be monitored monthly for survival information. All patients initially randomized to placebo were included in the placebo arm results, even if they crossed over to everolimus therapy after progression or unblinding. In total, 85% of patients in the placebo arm crossed over to everolimus during the course of the study.

The safety profile was consistent with that observed for Afinitor in advanced pancreatic NET and no unexpected or new safety concerns were identified at the time of the analysis.

Afinitor is approved in more than 85 countries including the U.S. and European Union for locally advanced, metastatic or unresectable progressive neuroendocrine tumors of pancreatic origin. It is also approved in more than 100 countries for advanced renal cell carcinoma following progression on or after vascular endothelial growth factor targeted therapy.

Novartis plans to submit this data to regulatory authorities for inclusion in Afinitor's prescribing information.

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Non-Small Cell Lung Cancer **Tecemotide Program Canceled Following Phase II Analysis**

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Of the patients included in the phase II part of the study, the majority had received concurrent CRT. No effect has been observed for either the primary endpoint of overall survival, or for any of the secondary endpoints, including progression-free survival, time to progression, and time to treatment failure.

An analysis of the reported adverse events has not identified a clinically meaningful difference in the frequency between treatment groups. Although the trial was not powered to demonstrate a statistically significant difference in benefit between the two arms, Merck Serono made the recommendation to stop the investigational treatment for patients in the EMR 63325-009 study.

“While the data from the exploratory subgroup analysis in the START trial generated a reasonable hypothesis to warrant additional study, the results of the recent trial in Japanese patients decreased the probability of current studies to reach their goals,” said Luciano Rossetti, global head of research and development at Merck Serono.

The START2 study is a 1:1 randomized, double-blind, placebo-controlled clinical trial in unresectable, stage IIIA or IIIB NSCLC who have had a response or stable disease after at least two cycles of platinum-based concurrent CRT.

The study, which began in April 2014, was expected to recruit about 1,000 patients.

The initial START study did not meet the primary endpoint of demonstrating an improved OS with tecemotide compared with placebo in the overall patient population (n=1,239). Median OS was 25.6 months for patients in the tecemotide group compared with 22.3 months for those in the placebo group (adjusted HR: 0.88; 95% CI: 0.75-1.03; p=0.123).

However, data from an exploratory analysis of a pre-defined subgroup of patients in the START trial—patients who received tecemotide after concurrent CRT—showed that these patients achieved a median OS of 30.8 months compared to 20.6 months in patients treated with placebo (n=806; HR: 0.78; 95% CI: 0.64-0.95; p=0.016).

INSPIRE is a multicenter, randomized, double-blind, placebo-controlled clinical trial in unresectable, locally advanced stage IIIA or IIIB NSCLC patients who have had a response or stable disease after at least

two cycles of platinum-based concurrent CRT. INSPIRE expected to recruit approximately 500 stage III NSCLC patients across China, Hong Kong, Korea, Singapore and Taiwan.

Patients on active treatment with tecemotide can undergo an individual assessment by their treating physician and apply to receive further treatment outside of the studies. Merck will continue to supply tecemotide for ongoing investigator-sponsored trials in other indications in accordance with the company's agreements with the sponsors of these studies.

Merck obtained the exclusive worldwide rights for development and commercialization of tecemotide from Oncothyreon Inc. in 2007, in an agreement replacing prior collaboration and supply agreements originally entered in 2001. In Japan, Merck entered into a co-development and co-marketing agreement for tecemotide with Ono Pharmaceutical Co., Ltd.

Gastric Cancer **Phase III Cyramza Trial Meets OS Primary Endpoint**

A global phase III trial of Cyramza (ramucirumab) in combination with paclitaxel in patients with advanced gastric cancer or gastroesophageal junction adenocarcinoma met its primary endpoint of median overall survival.

In the trial, known as RAINBOW, the addition of ramucirumab to paclitaxel also met secondary endpoints of progression-free survival and objective response rate. The global, double-blinded study enrolled a total of 665 patients refractory to or progressive after initial platinum- and fluoropyrimidine-containing chemotherapy.

Patients randomized to receive ramucirumab plus paclitaxel had a median survival benefit of 9.6 months, compared to 7.4 months for patients who received paclitaxel and placebo (stratified HR 0.807 [95% CI, 0.678-0.962; p=0.0169]).

Treatment with ramucirumab plus paclitaxel significantly reduced the risk of disease progression or death by 37 percent, with a 52 percent increase in median progression-free survival compared with placebo plus paclitaxel (4.4 vs. 2.9 months; stratified HR 0.635 [95% CI, 0.536-0.752; p < 0.0001]).

There was a statistically significant increase in objective response rate, from 16 to 28 percent, with the addition of ramucirumab (p=0.0001).

RAINBOW is the largest trial in second-line

gastric cancer to date and the first phase III study to demonstrate a survival benefit with a biologic used in combination with chemotherapy in this setting, according to the drug's sponsor, Eli Lilly and Company. Data were published in *The Lancet Oncology*, after being first presented at the Gastrointestinal Cancers Symposium in January.

Grade 3 or higher adverse events occurred at a higher rate and for more than 10 percent of patients on the ramucirumab-plus-paclitaxel arm: neutropenia; leukopenia; hypertension; and fatigue. Febrile neutropenia incidence was low in both trial arms, at 3 and 2 percent, respectively.

Cyramza is approved for use as a single agent in the U.S. for patients with advanced gastric 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.

There are several studies underway or planned to investigate Cyramza as a single agent and in combination with other anti-cancer therapies for the treatment of multiple tumor types.

Data from the RAINBOW trial are the basis for regulatory submissions in the U.S. and the European Union, according to Eli Lilly, and the company is planning a submission to Japanese regulatory authorities in the second half of 2014.

Colorectal Cancer

Phase III Xilonix Study Halted Following Unscheduled Analysis

An unscheduled interim analysis halted a fast-tracked phase III study of monoclonal antibody therapy Xilonix in advanced colorectal cancer patients with cachexia.

The primary endpoint of the study is overall survival, comparing survival in Xilonix treated patients to a control population provided only palliative therapy for cachexia.

Over half of the 40 patients enrolled in the trial have succumbed to disease. At the time of analysis, patients receiving Xilonix had a hazard ratio for risk of death of 0.33 ($p=0.11$) compared with controls. The strong hazard ratio reveals a marked trend for improved survival in the Xilonix treated group compared to controls, according to XBiotech, the drug's sponsor.

The unscheduled analysis was enabled due to a halt in the study for protocol amendments, which XBiotech says are intended to correct what are believed to be barriers to patient enrollment. The company says is currently collaborating with the FDA on revisions that will ensure the protocol remains suitable for biological licensing applications.

The new protocol is said to permit recruitment of all advanced refractory colorectal cancer patients and will be randomized 2:1 against placebo. XBiotech is expecting patients to be enrolled under the revised protocol as early as October.

XBiotech used the interim overall survival data in a model to predict the statistical significance of the survival benefit over the projected complete course of the study.

Key pharmacodynamic measures were also reported to be consistent with the intended biological activity of the therapy; as well, secondary endpoints evaluating quality of life were consistent with the observed survival benefit in Xilonix patients.

Ovarian Cancer

Cediranib/Olaparib Combination Nearly Doubles PFS in Phase II

A combination of cediranib and olaparib nearly doubled progression-free survival compared to olaparib alone in a phase II trial of patients with recurrent ovarian cancer.

The study enrolled 90 patients with platinum-sensitive ovarian cancer. Median PFS was nearly 18 months for women receiving the combined therapy, compared to nine months for those receiving olaparib.

In women whose ovarian tumors lacked mutations in the genes BRCA1 or BRCA2, the median PFS for those treated with the combination therapy was 16.5 months compared to 5.7 months for those treated with olaparib. In women whose tumors did carry BRCA mutations, the median PFS for the combined-therapy group was 19.4 months, compared to 16.5 for the olaparib group.

Severe side effects to treatment were more common in the cediranib-and-olaparib group, with fatigue, diarrhea, and hypertension the most frequent. Data from the study was published in *The Lancet Oncology*.

Two phase III clinical trials comparing the combination therapy to other drug regimens plan to begin enrolling patients early next year, and both will be

supported by NCI and run through the NRG Oncology cooperative group. One will compare cediranib and olaparib to chemotherapy in women with platinum-sensitive ovarian cancer. The other will compare olaparib alone, olaparib and cediranib, and chemotherapy in patients with platinum-resistant ovarian cancer.

Cediranib is an angiogenesis inhibitor, while Olaparib is a poly (ADP-ribose) polymerase inhibitor. Both drugs, used as single agents, had been shown to be active in women with recurrent ovarian cancers, and, as a pair, were found to be active and tolerable to patients in a phase I clinical trial.

This study was funded in part by NCI's Cancer Therapy Evolution Program and supported by an American Recovery and Reinvestment Act grant through NIH (3 U01 CA062490-16S2).

Chemotherapy

Fidaxomicin for CDI Therapy More Cost-Effective Than Vancomycin, Study Says

Overall treatment costs for cancer patients with clostridium difficile infection, based on a decision tree analysis, are lower with fidaxomicin compared to current standard of care, vancomycin, resulting in a potential cost saving of approximately \$7,000 per patient.

Patients who have received chemotherapy and those with solid tumors can be particularly susceptible to CDI due to their long hospital stays and exposure to many antibiotics and chemotherapeutic agents. These patients are also prone to recurrent episodes of CDI. Hospital patients with CDI are up to three times more likely to die in hospital (or within a month of infection) than those without CDI.

CDI results from infection of the internal lining of the colon by *C. difficile* bacteria. Patients typically develop CDI after the use of broad-spectrum antibiotics that disrupt normal bowel flora, allowing *C. difficile* bacteria to flourish.

This pharmacoeconomic model combined data from a study exploring the resolution of CDI in cancer patients treated with either fidaxomicin or vancomycin and a recent cost-of-illness analysis on CDI conducted at the University Hospital of Cologne.

The analysis explored direct cost parameters including drug costs, treatment on the general ward and intensive care unit as well as microbiological diagnostics for clostridium difficile.

Mean overall treatment costs per patient treated

with fidaxomicin and vancomycin were approximately \$28,000 and \$35,000, respectively. The lower costs were primarily due to the significantly lower rate of recurrence in patients treated with fidaxomicin.

Data were presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy.

"Patients with cancer represent a vulnerable population who are at high risk of CDI, often resulting from their compromised immune system. CDI can be a devastating addition for patients who are already battling pre-existing conditions," said lead investigator Sebastian Heimann, a health economist at the University Hospital of Cologne, Germany.

"We have already seen the superior reductions in CDI recurrence with fidaxomicin so we are pleased to see it also clearly demonstrating cost effectiveness."

NCI CTEP-Approved Trials For the Month of September

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

9605: Phase I Study of Ganetespib and Ziv-Afibercept in Patients with Advanced Gastrointestinal Carcinomas, Non-Squamous Non-Small Cell Lung Carcinomas, Urothelial Carcinomas, and Sarcomas. National Cancer Institute Developmental Therapeutics Clinic; Kummar, Shivaani. (301) 435-0517

AMC-091: Phase I and Pharmacokinetic Study of Ibrutinib in HIV-Infected Patients with Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma or Multiple Myeloma. AIDS-Associated Malignancies Clinical Trials Consortium; Kasamon, Yvette L. (410) 955-8839

Phase II

AOST1322: A Phase II Study of Eribulin (IND# 122686, NSC# 707389) in Recurrent or Refractory Osteosarcoma. Children's Oncology Group; Isakoff, Michael Scott. (860) 545-9630

Phase III

A081105: Randomized Double Blind Placebo Controlled Study of Erlotinib or Placebo in Patients with Completely Resected Epidermal Growth Factor Receptor (EGFR) Mutant Non-Small Cell Lung Cancer

(NSCLC). Alliance for Clinical Trials in Oncology; Govindan, Ramaswamy. (314) 362-5737

A221304: A Phase III Placebo-Controlled, Randomized Three-Arm Study of Doxepin and a Topical Rinse in the Treatment of Acute Oral Mucositis Pain in Patients Receiving Radiotherapy With or Without Chemotherapy. Alliance for Clinical Trials in Oncology; Miller, Robert C. (507) 284-2669

NRG-GI001: Randomized Phase III Study of Focal Radiation Therapy for Unresectable, Localized Intrahepatic Cholangiocarcinoma. NRG Oncology; Hong, Theodore Sunki. (617) 726-5866

Pilot Phase

9671: Exceptional Responders Pilot Study: Molecular Profiling of Tumors From Cancer Patients Who Are Exceptional Responders. National Institutes of Health; Conley, Barbara A. (240) 276-6505

WFU-01213: Reducing Lung Cancer Survivors' Anxiety and Dyspnea (RELAX). Wake Forest Cancer Center CCOP Research Base; Danhauer, Suzanne C. (336) 716-7980

Other Phases

A151308: Genetic Contributions to Symptom Reports: A Proposed Pilot Project. Alliance for Clinical Trials in Oncology; Sloan, Jeff A. (507) 284-9985

AALL14B5-Q: Identification of High Risk AIEOP Childhood ALL Cases with Targetable Fusion Transcripts. Children's Oncology Group; Cazzaniga, Giovanni. 39-0-39-233.2288.3661

ABTR14B2-Q: DDX3, A Novel Therapeutic Target in Sarcoma Ewing, Osteo and Rhabdomyosarcoma. Children's Oncology Group; Loeb, David M. (410) 502-7247

NRG-BN-TS002: Prognostic and Predictive Markers in Low-Grade Gliomas: A Study Based on RTOG 9802. NRG Oncology; Chakravarti, Arnab. (614) 293-3241

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FDA News

Keytruda Granted Approval In Metastatic Melanoma

FDA granted accelerated approval for Keytruda (pembrolizumab) for unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.

The indication was approved based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Keytruda received a Breakthrough Therapy designation for advanced melanoma, and is the first anti-programmed death receptor-1 therapy approved in the U.S.

The designation was granted based on the significance of early study findings and the unmet medical need. For the recommended 2 mg/kg dose based on data in 89 patients, the overall response rate was 24 percent (95% CI: 15, 34), with one complete response and 20 partial responses (21/89). At the time of analysis, 86 percent (18/21) of patients with objective responses had ongoing responses with durations ranging from 1.4+ to 8.5+ months, including eight patients with ongoing responses of 6 months or longer. Fourteen percent (3/21) had progression of disease 2.8, 2.9, and 8.2 months after initial response.

Keytruda is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, and may affect both tumor cells and healthy cells. Immune-mediated adverse reactions occurred with Keytruda including pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, and hypothyroidism.

Merck, the drug's sponsor, is conducting ongoing phase II and III clinical studies in advanced melanoma.

FDA approved a new indication for Xtandi (enzalutamide) capsules to treat patients with metastatic castration-resistant prostate cancer who have not received chemotherapy. This follows a priority review based on results of the phase III PREVAIL trial.

The agency initially approved Xtandi in August 2012 for use in patients with metastatic CRPC who previously received docetaxel.

In PREVAIL, men receiving Xtandi and GnRH therapy exhibited a statistically significant improvement in both overall survival and delayed time to radiographic progression or death as compared to those on placebo

and GnRH therapy. Xtandi significantly reduced the risk of radiographic progression or death by 83 percent compared with placebo (HR=0.17; $p < 0.0001$).

Xtandi significantly reduced the risk of death by 29 percent compared with placebo (HR=0.71; $p < 0.0001$). When compared to placebo, treatment with Xtandi also delayed time to initiation of chemotherapy and time to a skeletal related event.

Xtandi is sponsored by Medivation Inc. and Astellas Pharma Inc.

FDA removed separate clinical holds on trials involving two agents: one on **ipafricept**, developed by OncoMed Pharmaceuticals Inc.; and another on **PEGPH20**, sponsored by Halozyme Therapeutics Inc.

Ipafricept is being studied in combination with standard-of-care in three phase Ib studies. Enrollment and dosing of new patients is expected to resume within the next few weeks as the study sites' institutional review boards receive and approve the revised trial protocols.

“With important input from our clinical investigators and academic bone experts, the OncoMed team has developed modified study parameters intended to avoid potential risks while allowing us to evaluate the therapeutic impact of ipafricept for patients with pancreatic, hepatocellular and ovarian cancers in combination with standard therapy,” said Jakob Dupont, OncoMed's chief medical officer. The amendments for the combination trials include modified dosing regimens, risk mitigation measures, such as increased monitoring and bone protection strategies, and modified enrollment criteria.

OncoMed voluntarily halted enrollment in its vantiutumab and ipafricept Wnt pathway programs as a precautionary measure based on reported incidents of mild-to-moderate bone adverse events. The FDA concurred with the company's decision and placed the studies on partial clinical hold, allowing for the continued dosing of patients who demonstrated benefit without significant drug-related adverse effects.

Ipafricept is a first-in-class fusion protein that inhibits the Wnt pathway. Ipafricept selectively binds Wnt ligands that are activators of Wnt signaling. Ipafricept has shown broad anti-CSC and anti-tumor activity in patient-derived xenograft tumor models.

The ongoing Ib/II clinical trial evaluating PEGPH20 in combination with modified FOLFIRINOX chemotherapy in patients with metastatic pancreatic adenocarcinoma will also resume under a revised protocol.

The trial, which will enroll approximately 170 patients, is being sponsored by SWOG.

The phase Ib portion of the study will be a limited dose de-escalation clinical trial examining the dose-limiting toxicities in 6 to 18 patients, to identify the optimal dose for PEGPH20 used in combination with mFOLFIRINOX in patients with newly diagnosed metastatic pancreatic adenocarcinoma in the phase II portion of the study. The mFOLFIRINOX treatment regimen consists of oxaliplatin, leucovorin, irinotecan and 5-fluorouracil.

The phase II portion will be a randomized, multicenter, parallel arm study enrolling approximately 152 patients to yield 138 evaluable patients.

The study will also explore the treatment impact on carbohydrate antigen 19-9, a biomarker often associated with tumor cell burden, as well as the correlation of plasma hyaluronan and tumor HA with OS, PFS and ORR.

Soligenix Inc. reached an agreement with FDA on the design of a phase III clinical trial evaluating SGX301 (synthetic hypericin) for the treatment of cutaneous T-cell lymphoma.

The trial is anticipated to begin in the first half of 2015 with primary data available in the second half of 2016. SGX301 is a novel, first-in-class, photodynamic therapy that is topically applied to skin lesions and activated by visible fluorescent light.

The upcoming protocol will be a double-blind, randomized, placebo-controlled, multicenter trial that seeks to enroll approximately 120 patients. Treatments will be administered twice weekly for the first 6 weeks and treatment response will be determined at the end of Week 8.

In the first treatment cycle, approximately 80 patients will receive SGX301 and 40 will receive placebo treatment of their index lesions. In the second cycle, all patients will receive SGX301 treatment of their index lesions and in the third (open-label) cycle all patients will receive SGX301 treatment of all their lesions. Subjects will be followed for an additional 6 months after the completion of treatment.

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