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Alliance Foundation Trials Opens Global Trial Investigating First-in-Class Palbociclib in HR+, HER2+ Metastatic Breast Cancer

Tuesday, August 22, 2017 - 04:00am

Pfizer and International Cancer Research Groups collaborate on trial to evaluate new therapeutic combination

The Alliance Foundation Trials, LLC (AFT), in conjunction with Pfizer and six international cancer research groups, today announced the launch of PATINA – a randomized, open-label, Phase 3 clinical study of the cyclin-dependent kinase 4/6 (CDK 4/6) inhibitor palbociclib (also known as IBRANCE®). The PATINA trial will evaluate palbociclib in combination with anti-HER2 therapy and endocrine therapy versus standard therapy as a first-line treatment for patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer. The trial randomized its first patient on July 26, 2017.

“The PATINA trial offers an exciting opportunity for a new global collaborative initiative among clinical trial groups aimed at improving the treatment of women with metastatic breast cancer,” said Monica M. Bertagnolli, MD, President and Chief Executive Officer of Alliance Foundation Trials, LLC, and group chair and principal investigator of the Alliance for Clinical Trials in Oncology. “Our partnership with the Mastering Breast Cancer Initiative, PrECOG, the German Breast Group, Fondazione Michelangelo, SOLTI Breast Cancer Research Group and the Australia and New Zealand Breast Cancer Trials Group (ANZBCTG) makes this trial available to patients across the U.S., Europe, Australia and New Zealand. PATINA is the first study of the Mastering Breast Cancer Initiative which is an umbrella organization that includes multiple clinical trials whose participants will contribute medical information and biological specimens for future research. This initiative was created in order to understand the natural history of breast cancer and how it evolves over time with the overall goal to develop new treatments for this patient population.”

In the U.S., IBRANCE is indicated for the treatment of HR+, HER2-negative (HER2-) advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women, or fulvestrant in women with disease progression following endocrine therapy. Since its initial FDA approval in 2015, more than 60,000 patients have been treated with IBRANCE in the U.S. alone.

Pre-clinical data and preliminary results from early phase clinical trials point to the potential efficacy of palbociclib when combined with anti-HER2 therapies and endocrine therapy. About 10-15% of patients with metastatic breast cancer are HR+, HER2+.1 Palbociclib is currently not approved for use in this patient population in any country.

“The current PATINA study is built on strong pre-clinical and clinical rationale demonstrating the potential of palbociclib when given in combination with endocrine therapy and anti-HER2 therapies,” said Otto Metzger, MD, principal investigator of the trial for AFT and Medical Oncologist at the Dana-Farber Cancer Institute in

Boston. “We hope that this trial will show that the addition of palbociclib to the first-line treatment of HR+, HER2+ disease will help delay the onset of therapeutic resistance to endocrine therapy, complement the benefits of anti-HER2 therapy and ultimately improve patient outcomes. The study also includes a comprehensive molecular characterization of the disease when patients enter the study and at the time of disease progression.”

“We are pleased to partner with these prominent research groups to explore the use of palbociclib in first-line HR+, HER2+ disease,” said Charles Hugh-Jones, MD FRCP, Chief Medical Officer, Pfizer Oncology. “PATINA is the first randomized, Phase 3 trial of a CDK 4/6 inhibitor in this setting. Collaborations of this kind are critical to advance our understanding of how we can treat breast cancer, and they represent an important part of Pfizer’s clinical development program for palbociclib.”

The PATINA trial is a pivotal, open-label, international, multicenter, randomized Phase 3 study. The trial is open to women or men with HR+, HER2+ metastatic breast cancer following completion of induction with anti-HER2 based chemotherapy. Participants will be randomized (selected by chance) to one of two treatment arms following 6-8 cycles of chemotherapy with anti-HER2 therapy. One study arm will treat patients with palbociclib (at a dose of 125 mg orally once daily for 21 days followed by seven days off treatment in a 28-day cycle) and standard anti-HER2 therapy and endocrine therapy until disease progression. The other study arm will treat patients with standard anti-HER2 therapy and endocrine therapy until disease progression. About 500 participants will be recruited worldwide.

Alliance Foundation Trials, LLC, under the auspices of the Alliance for Clinical Trials in Oncology, has brought together a collaborative group of breast cancer specialists from around the world to team up with a pharmaceutical sponsor to form a public-private cancer research partnership aimed at bringing more innovative therapies to patients in more efficient ways.

For questions about this trial, please contact the PATINA study at patina@alliancefoundatiotrials.org.

Availability

Currently, the new study is open to physicians and medical facilities throughout the U.S. if they are associated with the Alliance Foundation and PrECOG oncology research groups. The study will be available to non-U.S. sites this fall through an extended academic core network that includes the German Breast Group (GBG), Fondazione Michelangelo, SOLTI Breast Cancer Research Group, and the Australia and New Zealand Breast Cancer Trials Group (ANZBCTG).

Information on the PATINA study can be found on the National Institutes of Health (NIH) registry of clinical trials, www.clinicaltrials.gov (Clinicaltrials.gov Identifier: NCT02947685), and on the PATINA website at www.patina-trial.com.

Funding and Sponsorship

Pfizer, the manufacturer of palbociclib (IBRANCE®), is providing funding support for this trial. AFT is the global sponsor of this trial which will be conducted in the U.S., Germany, Italy, Spain, Australia, and New Zealand.

About Alliance Foundation Trials, LLC

Alliance Foundation Trials, LCC (AFT), is a limited liability research organization that develops and conducts cancer clinical trials in all areas, working closely with industry partners. AFT is funded wholly by private entities and does not use any public funding resources. Its operational structure and clinical trials management

mechanism are separate from the Alliance for Clinical Trials in Oncology although AFT operates under its auspices. For more information about AFT, visit www.AllianceFoundationTrials.org.

About PrECOG

PrECOG is a not-for-profit limited liability company formed in 2006 by the ECOG Research and Education Foundation, Inc. Through this relationship, key opinion leaders and the entire network of the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN) investigators and institutions underpin PrECOG. Funded entirely outside of the public health system, PrECOG uses an operational structure separate from ECOG-ACRIN for all facets of clinical trial management. For more information, visit www.precogllc.org.

About German Breast Group (GBG)

GBG is an independent academic research organization founded in 2003 whose aims are the continuous improvement of breast cancer treatment and a nationwide increase in therapy quality. GBG comprises a network of 500 study centers and more than 1,000 study doctors, resulting in >50,000 enrolled patients so far in their clinical trials.

About SOLTI

SOLTI Breast Cancer Research Group is a nonprofit organization dedicated to clinical research in breast cancer. Established in 1995, the clinical trials performed by SOLTI are designed to answer questions of major scientific interest and clinical relevance.

About Fondazione Michelangelo

The Michelangelo Foundation is a nonprofit scientific foundation, officially recognized as a foundation since 1991. This foundation collaborates with Italian and international researchers to carry out innovative methods of study to improve cancer diagnosis and care systems. Michelangelo Foundation is particularly committed to training and dissemination of results of its research throughout the Italian and international medical community.

About Australia New Zealand Breast Cancer Trial Group (ANZBCTG)

The ANZBCTG is the largest independent breast cancer clinical trials research group in Australia and New Zealand. For almost 40 years, the ANZBCTG has conducted clinical trials for the treatment, prevention, and cure of breast cancer. The Group’s research program involves multicentre national and international clinical trials with more than 800 members at 90 institutions. It is committed to finding new and better treatments and prevention strategies for every person affected by breast cancer, the goal being to save lives today and in the future.

About Pfizer Oncology

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on those living with cancer. As a leader in oncology speeding cures and accessible breakthrough medicines to patients, Pfizer Oncology is helping to redefine life with cancer. Our strong pipeline of biologics, small molecules and immunotherapies, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments and licensing partners, Pfizer Oncology strives to cure or control cancer with its breakthrough medicines. Pfizer Oncology knows that success in oncology is not measured solely by the medicines you

manufacture, but rather by the meaningful partnerships you make to have a more positive impact on people's lives.

About IBRANCE® (palbociclib) 125 mg capsules

IBRANCE is an oral inhibitor of CDKs 4 and 6,2 which are key regulators of the cell cycle that trigger cellular progression.3,4 In the U.S., IBRANCE is indicated for the treatment of HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women, or fulvestrant in women with disease progression following endocrine therapy. Including the U.S., IBRANCE is approved in more than 65 countries.

Important IBRANCE (palbociclib) Safety Information from the U.S. Prescribing Information

Neutropenia was the most frequently reported adverse reaction in PALOMA-2 (80%) and PALOMA-3 (83%). In PALOMA-2, Grade 3 (56%) or 4 (10%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In PALOMA-3, Grade 3 (55%) or Grade 4 (11%) decreased neutrophil counts were reported in patients receiving IBRANCE plus fulvestrant. Febrile neutropenia has been reported in 1.8% of patients exposed to IBRANCE across PALOMA-2 and PALOMA-3. One death due to neutropenic sepsis was observed in PALOMA-3. Inform patients to promptly report any fever.

Monitor complete blood count prior to starting IBRANCE, at the beginning of each cycle, on Day 15 of first 2 cycles and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Based on the mechanism of action, IBRANCE can cause fetal harm. Advise females of reproductive potential to use effective contraception during IBRANCE treatment and for at least 3 weeks after the last dose. IBRANCE may impair fertility in males and has the potential to cause genotoxicity. Advise male patients with female partners of reproductive potential to use effective contraception during IBRANCE treatment and for 3 months after the last dose. Advise females to inform their healthcare provider of a known or suspected pregnancy. Advise women not to breastfeed during IBRANCE treatment and for 3 weeks after the last dose because of the potential for serious adverse reactions in nursing infants.

The most common adverse reactions (?10%) of any grade reported in PALOMA-2 for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (80% vs 6%), infections (60% vs 42%), leukopenia (39% vs 2%), fatigue (37% vs 28%), nausea (35% vs 26%), alopecia (33% vs 16%), stomatitis (30% vs 14%), diarrhea (26% vs 19%), anemia (24% vs 9%), rash (18% vs 12%), asthenia (17% vs 12%), thrombocytopenia (16% vs 1%), vomiting (16% vs 17%), decreased appetite (15% vs 9%), dry skin (12% vs 6%), pyrexia (12% vs 9%), and dysgeusia (10% vs 5%).

The most frequently reported Grade ?3 adverse reactions (?5%) in PALOMA-2 for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (66% vs 2%), leukopenia (25% vs 0%), infections (7% vs 3%), and anemia (5% vs 2%).

Lab abnormalities of any grade occurring in PALOMA-2 for IBRANCE plus letrozole vs placebo plus letrozole were decreased WBC (97% vs 25%), decreased neutrophils (95% vs 20%), anemia (78% vs 42%), decreased platelets (63% vs 14%), increased aspartate aminotransferase (52% vs 34%), and increased alanine aminotransferase (43% vs 30%).

The most common adverse reactions (?10%) of any grade reported in PALOMA-3 for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (83% vs 4%), leukopenia (53% vs 5%), infections (47%

vs 31%), fatigue (41% vs 29%), nausea (34% vs 28%), anemia (30% vs 13%), stomatitis (28% vs 13%), diarrhea (24% vs 19%), thrombocytopenia (23% vs 0%), vomiting (19% vs 15%), alopecia (18% vs 6%), rash (17% vs 6%), decreased appetite (16% vs 8%), and pyrexia (13% vs 5%).

The most frequently reported Grade ?3 adverse reactions (?5%) in PALOMA-3 for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (66% vs 1%) and leukopenia (31% vs 2%).

Lab abnormalities of any grade occurring in PALOMA-3 for IBRANCE plus fulvestrant vs placebo plus fulvestrant were decreased WBC (99% vs 26%), decreased neutrophils (96% vs 14%), anemia (78% vs 40%), decreased platelets (62% vs 10%), increased aspartate aminotransferase (43% vs 48%), and increased alanine aminotransferase (36% vs 34%).

Avoid concurrent use of strong CYP3A inhibitors. If patients must be administered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg/day. If the strong inhibitor is discontinued, increase the IBRANCE dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor. Grapefruit or grapefruit juice may increase plasma concentrations of IBRANCE and should be avoided. Avoid concomitant use of strong CYP3A inducers. The dose of sensitive CYP3A substrates with a narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure.

IBRANCE has not been studied in patients with moderate to severe hepatic impairment or in patients with severe renal impairment (CrCl <30 mL/min).

PFIZER DISCLOSURE NOTICE: The information contained in this release is as of August 22, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about IBRANCE (palbociclib), including a potential additional indication for the first-line treatment of patients with HR+, HER2+ metastatic breast cancer and its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of IBRANCE; the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any jurisdictions for the potential new indication and whether and when drug applications may be filed in any additional jurisdictions for IBRANCE for potential HR+/HER2- metastatic breast cancer indications or in any jurisdictions for any other potential indications for IBRANCE; whether and when any such other applications may be approved by regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of IBRANCE, including the potential additional indication; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer’s Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned “Risk Factors” and “Forward-Looking Information and Factors That May Affect Future Results”, as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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1 Loibl S, Gianni, L. HER2-positive breast cancer. Lancet. 2017; 389(10087): 2415-2429.

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3 Weinberg RA. pRb and Control of the Cell Cycle Clock. In: Weinberg RA, ed. The Biology of Cancer. 2nd ed. New York, NY: Garland Science; 2014:275-329.
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