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Pfizer Announces Positive Overall Survival in Phase 3 Trial of ADCETRIS® Regimen in Patients with Relapsed/? Refractory Diffuse Large B-cell Lymphoma (DLBCL)

Tuesday, March 12, 2024 - 06:45am

- *ECHELON-3 trial of ADCETRIS in combination with lenalidomide and rituximab showed significant improvement in primary endpoint of overall survival and in secondary endpoints of progression free survival and overall response rate versus lenalidomide and rituximab plus placebo, regardless of CD30 expression*
- *Pfizer to discuss regulatory submission with FDA, potentially leading to eighth indication for ADCETRIS*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced that a Phase 3 study of the antibody-drug conjugate ADCETRIS® (brentuximab vedotin) in combination with lenalidomide and rituximab for the treatment of patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) showed a statistically significant and clinically meaningful improvement in overall survival (OS) compared to lenalidomide and rituximab plus placebo. Positive outcomes were also observed in key secondary endpoints, including progression free survival (PFS) and overall response rate (ORR).

The safety and tolerability of ADCETRIS in the ECHELON-3 trial were consistent with what has been previously presented for patients with relapsed/refractory DLBCL treated with ADCETRIS in clinical trials. Full data will be submitted for presentation at an upcoming medical meeting.

“This is the third Phase 3 study in a type of lymphoma to demonstrate an overall survival benefit for an ADCETRIS combination. Based on the strong results from ECHELON-3, we’re excited that ADCETRIS could address an area of high unmet need in patients with relapsed or refractory DLBCL irrespective of CD30 expression,” said Roger Dansey, M.D., Chief Development Officer, Oncology, Pfizer. “The results are particularly encouraging because the study evaluated heavily pre-treated patients, including some who received prior CAR-T therapy.”

DLBCL is the most common type of lymphoma and is a fast-growing, aggressive blood cancer. Approximately 40% of patients with DLBCL do not respond to initial treatment or develop relapsed disease after first-line treatment.

ADCETRIS is a standard of care for patients with certain lymphomas and is approved for seven indications in the U.S with more than 55,000 patients treated since its first U.S. approval in 2011. More than 140,000 patients have been treated with ADCETRIS globally. Pfizer plans to share the ECHELON-3 data with the U.S. Food and Drug Administration (FDA) to potentially support regulatory filing in the U.S.

About ECHELON-3

ECHELON-3 is an ongoing, randomized, double-blind, multicenter Phase 3 study evaluating ADCETRIS plus lenalidomide and rituximab versus lenalidomide and rituximab plus placebo in adult patients with relapsed/refractory DLBCL, regardless of CD30 expression, who have received two or more prior lines of therapy and are ineligible for stem cell transplant or CAR-T therapy. In this global study, 230 patients were randomized across North America, Europe and Asia-Pacific. The primary endpoint is OS in the intent to treat population, with key secondary endpoints of PFS and ORR as assessed by investigator. Other secondary endpoints include complete response rate, duration of response, safety and tolerability.

About Diffuse Large B-cell Lymphoma

Diffuse large B-cell lymphoma (DLBCL) is the most frequent type of lymphoma and is an aggressive, difficult to treat disease.[1] More than 25,000 cases of DLBCL are diagnosed each year in the United States, accounting for more than 25 percent of all lymphoma cases.[2]

DLBCL can develop spontaneously or as a result of diseases such as chronic lymphocytic lymphoma/small lymphocytic lymphoma, follicular lymphoma, or marginal zone lymphoma.[3] Up to 40 percent of patients relapse or have refractory disease after frontline treatment.

About ADCETRIS

ADCETRIS is an antibody-drug conjugate (ADC) comprised of a CD30-directed monoclonal antibody attached by a protease-cleavable linker to a microtubule disrupting agent, monomethyl auristatin E (MMAE), utilizing Seagen's proprietary technology. The ADC employs a linker system that is designed to be stable in the bloodstream but to release MMAE upon internalization into CD30-positive tumor cells.

ADCETRIS is approved in seven indications in the U.S.:

- Adult patients with previously untreated Stage III/IV classical Hodkin lymphoma (cHL) in combination with doxorubicin, vinblastine, and dacarbazine (2018)
- Pediatric patients 2 years and older with previously untreated high risk cHL in combination with doxorubicin, vincristine, etoposide, prednisone and cyclophosphamide (2022)
- Adult patients with cHL at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation (2015)
- Adult patients with cHL after failure of auto-HSCT or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates (2011)
- Adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone (2018)
- Adult patients with sALCL after failure of at least one prior multi-agent chemotherapy regimen. (2011)
- Adult patients with primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) after prior systemic therapy (2017)

Pfizer and Takeda jointly develop ADCETRIS. Under the terms of the collaboration agreement, Pfizer has U.S. and Canadian commercialization rights, and Takeda has rights to commercialize ADCETRIS in the rest of the world. Pfizer and Takeda are funding joint development costs for ADCETRIS on a 50:50 basis, except in Japan where Takeda is solely responsible for development costs.

ADCETRIS® (brentuximab vedotin) for injection U.S. Important Safety Information

BOXED WARNING

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML): JC virus infection resulting in PML, and death can occur in ADCETRIS-treated patients.

CONTRAINDICATION

Contraindicated with concomitant bleomycin due to pulmonary toxicity (e.g., interstitial infiltration and/or inflammation).

WARNINGS AND PRECAUTIONS

Peripheral neuropathy (PN): ADCETRIS causes PN that is predominantly sensory. Cases of motor PN have also been reported. ADCETRIS-induced PN is cumulative. Monitor for symptoms such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness. Patients experiencing new or worsening PN may require a delay, change in dose, or discontinuation of ADCETRIS.

Anaphylaxis and infusion reactions: Infusion-related reactions (IRR), including anaphylaxis, have occurred with ADCETRIS. Monitor patients during infusion. If an IRR occurs, interrupt the infusion and institute appropriate medical management. If anaphylaxis occurs, immediately and permanently discontinue the infusion and administer appropriate medical therapy. Premedicate patients with a prior IRR before subsequent infusions. Premedication may include acetaminophen, an antihistamine, and a corticosteroid.

Hematologic toxicities: Fatal and serious cases of febrile neutropenia have been reported with ADCETRIS. Prolonged (?1 week) severe neutropenia and Grade 3 or 4 thrombocytopenia or anemia can occur with ADCETRIS.

Administer G-CSF primary prophylaxis beginning with Cycle 1 for adult patients who receive ADCETRIS in combination with chemotherapy for previously untreated Stage III/IV cHL or previously untreated PTCL, and pediatric patients who receive ADCETRIS in combination with chemotherapy for previously untreated high risk cHL.

Monitor complete blood counts prior to each ADCETRIS dose. Monitor more frequently for patients with Grade 3 or 4 neutropenia. Monitor patients for fever. If Grade 3 or 4 neutropenia develops, consider dose delays, reductions, discontinuation, or G-CSF prophylaxis with subsequent doses.

Serious infections and opportunistic infections: Infections such as pneumonia, bacteremia, and sepsis or septic shock (including fatal outcomes) have been reported in ADCETRIS-treated patients. Closely monitor patients during treatment for infections.

Tumor lysis syndrome: Patients with rapidly proliferating tumor and high tumor burden may be at increased risk. Monitor closely and take appropriate measures.

Increased toxicity in the presence of severe renal impairment: The frequency of ?Grade 3 adverse reactions and deaths was greater in patients with severe renal impairment. Avoid use in patients with severe renal impairment.

Increased toxicity in the presence of moderate or severe hepatic impairment: The frequency of ?Grade 3 adverse reactions and deaths was greater in patients with moderate or severe hepatic impairment. Avoid use in patients with moderate or severe hepatic impairment.

Hepatotoxicity: Fatal and serious cases have occurred in ADCETRIS-treated patients. Cases were consistent with hepatocellular injury, including elevations of transaminases and/or bilirubin, and occurred after the first ADCETRIS dose or rechallenge. Preexisting liver disease, elevated baseline liver enzymes, and concomitant medications may increase the risk. Monitor liver enzymes and bilirubin. Patients with new, worsening, or recurrent hepatotoxicity may require a delay, change in dose, or discontinuation of ADCETRIS.

PML: Fatal cases of JC virus infection resulting in PML have been reported in ADCETRIS-treated patients. First onset of symptoms occurred at various times from initiation of ADCETRIS, with some cases occurring within 3 months of initial exposure. In addition to ADCETRIS therapy, other possible contributory factors include prior therapies and underlying disease that may cause immunosuppression. Consider PML diagnosis in patients with new-onset signs and symptoms of central nervous system abnormalities. Hold ADCETRIS if PML is suspected and discontinue ADCETRIS if PML is confirmed.

Pulmonary toxicity: Fatal and serious events of noninfectious pulmonary toxicity, including pneumonitis, interstitial lung disease, and acute respiratory distress syndrome, have been reported. Monitor patients for signs and symptoms, including cough and dyspnea. In the event of new or worsening pulmonary symptoms, hold ADCETRIS dosing during evaluation and until symptomatic improvement.

Serious dermatologic reactions: Fatal and serious cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with ADCETRIS. If SJS or TEN occurs, discontinue ADCETRIS and administer appropriate medical therapy.

Gastrointestinal (GI) complications: Fatal and serious cases of acute pancreatitis have been reported. Other fatal and serious GI complications include perforation, hemorrhage, erosion, ulcer, intestinal obstruction, enterocolitis, neutropenic colitis, and ileus. Lymphoma with pre-existing GI involvement may increase the risk of perforation. In the event of new or worsening GI symptoms, including severe abdominal pain, perform a prompt diagnostic evaluation and treat appropriately.

Hyperglycemia: Serious cases, such as new-onset hyperglycemia, exacerbation of pre-existing diabetes mellitus, and ketoacidosis (including fatal outcomes) have been reported with ADCETRIS. Hyperglycemia occurred more frequently in patients with high body mass index or diabetes. Monitor serum glucose and if hyperglycemia develops, administer anti-hyperglycemic medications as clinically indicated.

Embryo-fetal toxicity: Based on the mechanism of action and animal studies, ADCETRIS can cause fetal harm. Advise females of reproductive potential of this potential risk, and to use effective contraception during ADCETRIS treatment and for 2 months after the last dose of ADCETRIS. Advise male patients with female partners of reproductive potential to use effective contraception during ADCETRIS treatment and for 4 months after the last dose of ADCETRIS.

ADVERSE REACTIONS

The most common adverse reactions (?20% in any study) are peripheral neuropathy, fatigue, nausea, diarrhea, neutropenia, upper respiratory tract infection, pyrexia, constipation, vomiting, alopecia, decreased weight, abdominal pain, anemia, stomatitis, lymphopenia, mucositis, thrombocytopenia, and febrile neutropenia.

DRUG INTERACTIONS

Concomitant use of strong CYP3A4 inhibitors has the potential to affect the exposure to monomethyl auristatin E (MMAE). Closely monitor adverse reactions.

USE IN SPECIAL POPULATIONS

Lactation: Breastfeeding is not recommended during ADCETRIS treatment.

Please see the full Prescribing Information, including BOXED WARNING, for ADCETRIS here.

About Pfizer Oncology

At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes game-changing mechanisms of action to attack cancer from multiple angles, including antibody-drug conjugates (ADCs), small molecules, bispecific antibodies and other immunotherapy biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to extend and improve patients' lives.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety, and value in the discovery, development, and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments, and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments, and local communities to support and expand access to reliable, affordable health care around the world. For more than 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on X at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Disclosure Notice

The information contained in this release is as of March 12, 2024. 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 Pfizer Oncology and ADCETRIS (brentuximab vedotin), including its potential benefits, its potential for relapsed/refractory diffuse large B-cell lymphoma (DLBCL), potential for a regulatory filing in the U.S. and the ongoing investigational trial for ADCETRIS in combination with lenalidomide and rituximab, 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 ADCETRIS; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; 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 particular jurisdictions for ADCETRIS with lenalidomide and rituximab or as a single agent for any potential indication; whether and when any applications that may be pending or filed for ADCETRIS, may be approved by regulatory authorities, which will depend on

myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether ADCETRIS with lenalidomide and rituximab or as a single agent will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of ADCETRIS with lenalidomide and rituximab or as a single agent; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; 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, 2023 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.

[1] National Library of Medicine. Diffuse Large B-Cell Lymphoma. https://www.ncbi.nlm.nih.gov/books/NBK557796/. Updated April 24, 2023.
[2] Leukemia & Lymphoma Society. Diffuse Large B-Cell Lymphoma (DLBCL). https://www.lls.org/research/diffuse-large-b-cell-lymphoma-dlbcl
[3] National Library of Medicine. Diffuse Large B-Cell Lymphoma. https://www.ncbi.nlm.nih.gov/books/NBK557796/. Updated April 24, 2023.
[4] Duarte C, Kamdar M. "Management Considerations for Patients With Primary Refractory and Early Relapsed Diffuse Large B-Cell Lymphoma." American Society of Clinical Oncology. https://doi.org/10.1200/EDBK_390802. April 25, 2023

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