FDA Approves Drug Combination for Treating Mesothelioma

First approval in 16 years for mesothelioma, a type of cancer caused by inhaling asbestos fibers

Today, the U.S. Food and Drug Administration approved Opdivo (nivolumab) in combination with Yervoy (ipilimumab) for the first-line treatment of adults with malignant pleural mesothelioma that cannot be removed by surgery. This is the first drug regimen approved for mesothelioma in 16 years and the second FDA-approved systemic therapy for mesothelioma.

"Today's approval of nivolumab plus ipilimumab provides a new treatment that has demonstrated an improvement in overall survival for patients with malignant pleural mesothelioma," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "In 2004, FDA approved pemetrexed in combination with cisplatin for this indication, and now patients now have an important, additional treatment option after more than a decade with only one FDA-approved drug regimen."

Malignant pleural mesothelioma (MPM) is a life-threatening cancer of the lungs' lining caused by inhaling asbestos fibers that about 20,000 Americans are diagnosed with each year. MPM accounts for most mesothelioma diagnoses, and most patients have an unresectable (unable to be removed with surgery) tumor at time of diagnosis. With currently available therapy, overall survival is generally poor. Opdivo and Yervoy are both monoclonal antibodies that, when combined, decrease tumor growth by enhancing T-cell function.

This combination therapy was evaluated during a randomized, open-label trial in 605 patients with previously untreated unresectable MPM. Patients received intravenous infusions of Opdivo every two weeks with intravenous infusions of Yervoy every six weeks for up to two years, or platinum-doublet chemotherapy for up to six cycles. Treatment continued until disease progression, unacceptable toxicity or completion of two years. The objective was to determine if Opdivo in combination with Yervoy improved overall survival compared to chemotherapy. At the time of the analysis, patients who received Opdivo in combination with Yervoy survived a median of 18.1 months while patients who underwent chemotherapy survived a median of 14.1 months.

The most common side effects of Opdivo in combination with Yervoy in patients with MPM include: fatigue, musculoskeletal pain, rash, diarrhea, dyspnea (difficulty breathing), nausea, decreased appetite, cough and pruritis (itching). Yervoy can cause serious conditions known as immune-mediated side effects, including inflammation of healthy organs, such as the lungs (pneumonitis), colon (colitis), liver (hepatitis), endocrine glands (endocrinopathies) and kidneys (nephritis). Patients should tell their healthcare providers if they have immune system problems, lung or breathing problems, liver problems, have had an organ transplant, or are pregnant or plan to become pregnant before starting treatment.

The FDA granted approval to Bristol-Myers Squibb Company.

This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, FDA collaborated with the Australian Therapeutic Goods Administration (TGA), the Brazilian Health Regulatory Agency (ANVISA), Health Canada, and Switzerland's Swissmedic. The application reviews are ongoing at the other regulatory agencies. FDA approval occurred approximately 5 months ahead of the goal date.

FDA News released Oct 2, 2020. www.fda.gov.

FDA Approves First Treatment for Ebola Virus

Today, the U.S. Food and Drug Administration approved Inmazeb (atoltivimab, maftivimab, and odesivimab-ebgn), a mixture of three monoclonal antibodies, as the first FDA-approved treatment for Zaire ebolavirus (Ebola virus) infection in adult and pediatric patients.

"Today's action demonstrates the FDA's ongoing commitment to responding to public health threats—both domestically and abroad—on the basis of science and data," said FDA Commissioner Stephen M. Hahn, M.D. "This approval was made possible because of our steadfast dedication to facilitate the development of safe and effective treatments for infectious diseases as part of our vital public health mission."

Zaire ebolavirus, commonly known as Ebola virus, is one of four Ebolavirus species that can cause a potentially fatal human disease. Ebola virus is transmitted through direct contact with blood, body fluids and tissues of infected people or wild animals, as well as with surfaces and materials, such as bedding and clothing, contaminated with these fluids. Individuals who provide care for people with Ebola virus, including health care workers who do not use correct infection control precautions, are at the highest risk for infection.

Inmazeb targets the glycoprotein that is on the surface of Ebola virus. Glycoprotein attaches to the cell receptor and fuses the viral and host cell membranes allowing the virus to enter the cell. The three antibodies that make up Inmazeb can bind to this glycoprotein simultaneously and block attachment and entry of the virus.

Inmazeb was evaluated in 382 adult and pediatric patients with confirmed Zaire ebolavirus infection in one clinical trial (the PALM trial) and as part of an expanded access program conducted in the Democratic Republic of the Congo (DRC) during an Ebola virus outbreak in 2018-2019. The PALM trial was led by the U.S. National Institutes of Health and the DRC's Institut National de Recherche Biomédicale with contributions from several other international organizations and agencies.

"Today's approval highlights the importance of international collaboration in the fight against Ebola virus," said John Farley, M.D., MPH, director of the Office of Infectious Diseases in the FDA's Center for Drug Evaluation and Research. "The urgent need for advanced therapies to combat this infectious disease is clear, and today's action is a significant step forward in that effort."

In the PALM trial, the safety and efficacy of Inmazeb was evaluated in a multi-center, open-label, randomized controlled trial, in which 154 patients received Inmazeb (50 mg of each monoclonal antibody) intravenously as a single infusion, and 168 patients received an investigational control. The primary efficacy endpoint was 28-day mortality. The primary analysis population was all patients who were randomized and concurrently eligible to receive either Inmazeb or the investigational control during the same time period of the trial. Of the 154 patients who received Inmazeb, 33.8% died after 28 days, compared to 51% of the 153 patients who received a control. In the expanded access program, an additional 228 patients received Inmazeb.

The most common symptoms experienced while receiving Inmazeb included: fever, chills, tachycardia (fast heart rate), tachypnea (fast breathing), and vomiting; however, these are also common symptoms of Ebola virus infection. Patients who receive Inmazeb should avoid the concurrent administration of a live vaccine due to the treatment's potential to inhibit replication of a live vaccine virus indicated for prevention of Ebola virus infection and possibly reduce the vaccine's efficacy.

Hypersensitivity, including infusion-related events, can occur in patients taking Inmazeb, and treatment should be discontinued in the event of a hypersensitivity reaction.

Inmazeb received an Orphan Drug designation for the treatment of Ebola virus infection. The Orphan Drug designation provides incentives to assist and encourage drug development for rare diseases. Additionally, the agency granted Inmazeb a Breakthrough Therapy designation for the treatment of Zaire ebolavirus infection.

The FDA is granting the approval to Regeneron Pharmaceuticals.

The FDA approved Ervebo, the first vaccine for the prevention of Ebola virus disease, in December 2019, with support from a study conducted in Guinea during the 2014-2016 Ebola outbreak.

FDA News released Oct 14, 2020. www.fda.gov.

FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine

Action Follows Thorough Evaluation of Available Safety, Effectiveness, and Manufacturing Quality Information by FDA Career Scientists, Input from Independent Experts

Today, the U.S. Food and Drug Administration issued the first emergency use authorization (EUA) for a vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The emergency use authorization allows the Pfizer-BioNTech COVID-19 Vaccine to be distributed in the U.S.

"The FDA's authorization for emergency use of the first COVID-19 vaccine is a significant milestone in battling this devastating pandemic that has affected so many families in the United States and around the world," said FDA Commissioner Stephen M. Hahn, M.D. "Today's action follows an open and transparent review process that included input from independent scientific and public health experts and a thorough evaluation by the agency's career scientists to ensure this vaccine met FDA's rigorous, scientific standards for safety, effectiveness, and manufacturing quality needed to support emergency use authorization. The tireless work to develop a new vaccine to prevent this novel, serious, and life-threatening disease in an expedited timeframe after its emergence is a true testament to scientific innovation and public-private collaboration worldwide."

The FDA has determined that Pfizer-BioNTech COVID-19 Vaccine has met the statutory criteria for issuance of an EUA. The totality of the available data provides clear evidence that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19. The data also support that the known and potential benefits outweigh the known and potential risks, supporting the vaccine's use in millions of people 16 years of age and older, including healthy individuals. In making this determination, the FDA can assure the public and medical community that it has conducted a thorough evaluation of the available safety, effectiveness and manufacturing quality information.

The Pfizer-BioNTech COVID-19 Vaccine contains messenger RNA (mRNA), which is genetic material. The vaccine contains a small piece of the SARS-CoV-2 virus's mRNA that instructs cells in the body to make the virus's distinctive "spike" protein. When a person receives this vaccine, their body produces copies of the spike protein, which does not cause disease, but triggers the immune system to learn to react defensively, producing an immune response against SARS-CoV-2.

"While not an FDA approval, today's emergency use authorization of the Pfizer-BioNTech COVID-19 Vaccine holds the promise to alter the course of this pandemic in the United States," said Peter Marks, M.D., Ph.D., Director of the FDA's Center for Biologics Evaluation and Research. "With science guiding our decision-making, the available safety and effectiveness data support the authorization of the Pfizer-BioNTech COVID-19 Vaccine because the vaccine's known and potential benefits clearly outweigh its known and potential risks. The data provided by the sponsor have met the FDA's expectations as conveyed in our June and October guidance documents. Efforts to speed vaccine development have not sacrificed scientific standards or the integrity of our vaccine evaluation process. The FDA's review process also included public and independent review from members of the agency's Vaccines and Related Biological Products Advisory Committee. Today's achievement is ultimately a testament to the commitment of our career scientists and physicians, who worked tirelessly to thoroughly evaluate the data and information for this vaccine."

FDA Evaluation of Available Safety Data

Pfizer BioNTech COVID-19 Vaccine is administered as a series of two doses, three weeks apart. The available safety data to support the EUA include 37,586 of the participants enrolled in an ongoing randomized, placebo-controlled international study, the majority of whom are U.S. participants. These participants, 18,801 of whom received the vaccine and 18,785 of whom received saline placebo, were followed for a median of two months after receiving the second dose. The most commonly reported side effects, which typically lasted several days, were pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, and fever. Of note, more people experienced these side effects after the second dose than after the first dose, so it is important for vaccination providers and recipients to expect that there may be some side effects after either dose, but even more so after the second dose.

It is mandatory for Pfizer Inc. and vaccination providers to report the following to the Vaccine Adverse Event Reporting System (VAERS) for Pfizer-BioNTech COVID-19 Vaccine: all vaccine administration errors, serious adverse events, cases of Multisystem Inflammatory Syndrome (MIS), and cases of COVID-19 that result in hospitalization or death.

FDA Evaluation of Available Effectiveness Data

The effectiveness data to support the EUA include an analysis of 36,523 participants in the ongoing randomized, placebo-controlled international study, the majority of whom are U.S. participants, who did not have evidence of SARS-CoV-2 infection through seven days after the second dose. Among these participants, 18,198 received the vaccine and 18,325 received placebo. The vaccine was 95% effective in preventing COVID-19 disease among these clinical trial participants with eight COVID-19 cases in the vaccine group and 162 in the placebo group. Of these 170 COVID-19 cases, one in the vaccine group and three in the placebo group were

classified as severe. At this time, data are not available to make a determination about how long the vaccine will provide protection, nor is there evidence that the vaccine prevents transmission of SARS-CoV-2 from person to person.

The EUA Process

On the basis of the determination by the Secretary of the Department of Health and Human Services on February 4, 2020, that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and then issued declarations that circumstances exist justifying the authorization of emergency use of unapproved products, the FDA may issue an EUA to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent COVID-19 when there are no adequate, approved, and available alternatives.

The issuance of an EUA is different than an FDA approval (licensure) of a vaccine. In determining whether to issue an EUA for a product, the FDA evaluates the available evidence and assesses any known or potential risks and any known or potential benefits, and if the benefit-risk assessment is favorable, the product is made available during the emergency. Once a manufacturer submits an EUA request for a COVID-19 vaccine to the FDA, the agency then evaluates the request and determines whether the relevant statutory criteria are met, taking into account the totality of the scientific evidence about the vaccine that is available to the FDA.

The EUA also requires that fact sheets that provide important information, including dosing instructions, and information about the benefits and risks of the Pfizer-BioNTech COVID-19 Vaccine, be made available to vaccination providers and vaccine recipients.

The company has submitted a pharmacovigilance plan to FDA to monitor the safety of Pfizer-BioNTech COVID-19 Vaccine. The pharmacovigilance plan includes a plan to complete longer-term safety follow-up for participants enrolled in ongoing clinical trials. The pharmacovigilance plan also includes other activities aimed at monitoring the safety profile of the Pfizer-BioNTech COVID-19 vaccine and ensuring that any safety concerns are identified and evaluated in a timely manner.

The FDA also expects manufacturers whose COVID-19 vaccines are authorized under an EUA to continue their clinical trials to obtain additional safety and effectiveness information and pursue approval (licensure).

The EUA for the Pfizer-BioNTech COVID-19 Vaccine was issued to Pfizer Inc. The EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19 is terminated, and may be revised or revoked if it is determined the EUA no longer meets the statutory criteria for issuance.

FDA News released Dec 11, 2020. www.fda.gov.

Source: FDA