Jazz Pharmaceuticals Announces Update to National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology for Biliary Tract Cancers to Include zanidatamab-hrii (Ziihera®)

December 05, 2024

Ziihera, the first and only FDA-approved dual HER2-targeted bispecific antibody for HER2+ (IHC 3+) BTC, is now commercially available in the United States

For U.S. media and investors only

DUBLIN, Dec. 5, 2024 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that zanidatamab-hrii (Ziihera®) 50 mg/mL for injection for intravenous use is recommended by the National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a category 2A treatment option for Biliary Tract Cancers (BTC).

Ziihera was granted accelerated approval by the U.S. Food and Drug Administration (FDA) on November 20, 2024, for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test. The FDA approval of *Ziihera* was based on results from the HERIZON-BTC-01 clinical trial including a 52% objective response rate and median duration of response of 14.9 months as determined by independent central review (ICR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.[1] *Ziihera* is now commercially available to prescribers and customers in the U.S. and is available for purchase from authorized Specialty Distributors.

"The addition of *Ziihera* to the NCCN Guidelines® in Oncology reaffirms the importance of this advancement in treating BTC and supports our commitment to ensuring that HER2-positive BTC patients, through their health care professionals, can access this important new therapeutic option," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development, and chief medical officer of Jazz Pharmaceuticals. "*Ziihera* is the first and only dual HER2-targeted bispecific antibody and chemotherapy-free treatment for patients living with BTC – a disease with a poor prognosis and limited treatment options. We are excited to deliver this new treatment option to patients in the United States following its accelerated approval."

The NCCN Guidelines play a pivotal role in decision-making processes for individuals involved in cancer care all over the world, including physicians, nurses, pharmacists, payers, and patients and their families. The guidelines present expert recommendations for cancer screening, diagnosis and treatment, as well as cancer care options, and is utilized in cancer treatment decision-making to drive positive patient outcomes.

The NCCN is a not-for-profit alliance of 33 leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to defining and advancing quality, effective, equitable, and accessible cancer care and prevention so all people can live better lives.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

More information about *Ziihera*, the Full Prescribing Information, including Boxed Warning and Patient Information, is available **here**.

About Ziihera® (zanidatamab-hrii)
Ziihera (zanidatamab-hrii) is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Binding of zanidatamab-hrii with HER2 results in internalization leading to a reduction of the receptor on the tumor cell surface. Zanidatamab-hrii induces complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). These mechanisms result in tumor growth inhibition and cell death in vitro and in vivo.[1] In the United States, *Ziihera* is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test.[1] The U.S. Food and Drug Administration (FDA) granted accelerated approval for this indication based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).[1]

Zanidatamab is not approved anywhere else in the world.

Zanidatamab is being developed in multiple clinical trials as a targeted treatment option for patients with solid tumors that express HER2. Zanidatamab is being developed by Jazz and BeiGene, Ltd. (BeiGene) under license agreements from Zymeworks, which first developed the molecule.

The FDA granted Breakthrough Therapy designation for zanidatamab development in patients with previously treated HER2-amplified BTC, and two Fast Track designations for zanidatamab: one as a single agent for refractory BTC and one in combination with standard-of-care chemotherapy for first line gastroesophageal adenocarcinoma (GEA). Additionally, zanidatamab has received Orphan Drug designations from FDA for the treatment of BTC and GEA, as well as Orphan Drug designation from the European Medicines Agency for the treatment of BTC and gastric cancer.

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY
Exposure to ZIIHERA during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity
ZIIHERA can cause fetal harm when administered to a pregnant woman. In literature reports, use of a HER2-directed antibody during pregnancy resulted in cases of oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death.

Verify the pregnancy status of females of reproductive potential prior to the initiation of ZIIHERA. Advise pregnant women and females of reproductive potential that exposure to ZIIHERA during pregnancy or within 4 months prior to conception can result in fetal harm. Advise females of reproductive potential to use effective contraception during treatment with ZIIHERA and for 4 months following the last dose of ZIIHERA.

Left Ventricular Dysfunction
ZIIHERA can cause decreases in left ventricular ejection fraction (LVEF). LVEF declined by >10% and decreased to <50% in 4.3% of 233 patients. Left ventricular dysfunction (LVD) leading to permanent discontinuation of ZIIHERA was reported in 0.9% of patients. The median time to first occurrence of LVD was 5.6 months (range: 1.6 to 18.7). LVD resolved in 70% of patients.

Assess LVEF prior to initiation of ZIIHERA and at regular intervals during treatment. Withhold dose or permanently discontinue ZIIHERA based on severity of adverse reactions.

The safety of ZIIHERA has not been established in patients with a baseline ejection fraction that is below 50%.

Infusion-Related Reactions
ZIIHERA can cause infusion-related reactions (IRRs). An IRR was reported in 31% of 233 patients treated with ZIIHERA as a single agent in clinical studies, including Grade 3 (0.4%), and Grade 2 (25%). IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.4% of patients. IRRs occurred on the first day of dosing in 28% of patients; 97% of IRRs resolved within one day.

Prior to each dose of ZIIHERA, administer premedications to prevent potential IRRs. Monitor patients for signs and symptoms of IRR during ZIIHERA administration and as clinically indicated after completion of infusion. Have medications and emergency equipment to treat IRRs available for immediate use.

If an IRR occurs, slow, or stop the infusion, and administer appropriate medical management. Monitor patients until complete resolution of signs and symptoms before resuming. Permanently discontinue ZIIHERA in patients with recurrent severe or life-threatening IRRs.

Diarrhea
ZIIHERA can cause severe diarrhea.

Diarrhea was reported in 48% of 233 patients treated in clinical studies, including Grade 3 (6%) and Grade 2 (17%). If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Withhold or permanently discontinue ZIIHERA based on severity.

ADVERSE REACTIONS
Serious adverse reactions occurred in 53% of 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA. Serious adverse reactions in >2% of patients included biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhea (3.8%), gastric obstruction (3.8%), and fatigue (2.5%). A fatal adverse reaction of hepatic failure occurred in one patient who received ZIIHERA.

The most common adverse reactions in 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA (≥20%) were diarrhea (50%), infusion-related reaction (35%), abdominal pain (29%), and fatigue (24%).

USE IN SPECIFIC POPULATIONS

Pediatric Use
Safety and efficacy of ZIIHERA have not been established in pediatric patients.

Geriatric Use
Of the 80 patients who received ZIIHERA for unresectable or metastatic HER2-positive BTC, there were 39 (49%) patients 65 years of age and older. Thirty-seven (46%) were aged 65-74 years old and 2 (3%) were aged 75 years or older.

No overall differences in safety or efficacy were observed between these patients and younger adult patients.

About Biliary Tract Cancer
BTC, including gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, account for <1% of all adult cancers globally and are often associated with a poor prognosis.[2,3] The human epidermal growth factor receptor 2 (HER2) is a well-validated target for antitumor therapy in other cancers. Across the U.S., Europe, and Japan, approximately 12,000 people are diagnosed with HER2+ BTC annually.[4,5,6,7]

About Jazz Pharmaceuticals
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharma company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases—often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit www.jazzpharmaceuticals.com for more information.

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[1] ZIIHERA (zanidatamab-hrii) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

[2] Valle JW, et al. Lancet 2021; 397:428-44

[3] Siegel RL, et al. CA Cancer J Clin 2022; 72;7-33

[4] BTC overall diagnosed patients as per SEER 22.

[5] Assumes anatomic subsites intrahepatic CCA, extrahepatic CCA, gallbladder cancer, and BTC unspecified.

[6] Assumes HER2 positivity rates per anatomical subsite from Galdy, S., Lamarca, A., McNamara, M.G. et al. Cancer Metastasis Rev 36, 141–157 (2017), Nobuyoshi Hiraoka, et al. Human Pathology, Volume 105, 2020, Pages 9-19

[7] Major markets: UK, France, Germany, Spain, Italy. Note: HER2+ BTC patients in Jazz-controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd



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SOURCE Jazz Pharmaceuticals plc