ZIIHERA®
(zanidatamab-hrii)
50 mg/ml Injection for IV

IDENTIFYING PATIENTS WITH HER2 POSITIVITY FOR ZIIHERA

HER2 is an actionable biomarker in biliary tract cancer, which includes gallbladder cancer and intra- and extrahepatic cholangiocarcinoma.[1]

INDICATION

ZIIHERA (zanidatamab-hrii) 50 mg/mL for Injection for IV 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.

This indication is approved under accelerated approval 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).

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.

HER2=human epidermal growth factor receptor 2; IHC=immunohistochemistry.

NCCN RECOMMENDS ZANIDATAMAB-HRII (ZIIHERA)

ZANIDATAMAB-HRII (ZIIHERA) is recommended by the National Comprehensive Cancer Network® (NCCN®) as an NCCN Category 2A option for the subsequent-line systemic treatment of patients with HER2-positive (IHC 3+) unresectable or metastatic biliary tract cancer upon disease progression[2]

Please see additional Important Safety Information throughout and full Prescribing Information, including BOXED Warning.

IMPROVED OUTCOMES START WITH TESTING AT DIAGNOSIS[3,4]

UP TO 31% OF PATIENTS with biliary tract cancer have HER2 overexpression, a key driver of tumor growth.[2,5]

HER2 POSITIVITY BY BILIARY TRACT CANCER SUBTYPE[6]

31% Gallbladder

26% Cholangiocarcinomas*

HER2-targeted treatment significantly improved outcomes in patients with HER2-positive biliary tract cancer.[7†]

IT IS RECOMMENDED TO TEST FOR HER2 WITH BOTH IHC AND NGS

IHC is the standard method for detecting HER2 overexpression. NGS can detect HER2 amplification and other biomarkers, and can analyze cfDNA in liquid biopsies when tissue is limited. **Testing with both modalities, starting with IHC when possible, may reduce the risk of missed HER2-positive patients.[2,8-11]**

HER2 OVEREXPRESSION

IHC

- Detects and quantifies HER2 protein overexpression in tissue samples[8]
- Results: 3+ (positive), 2+ (equivocal), 0/1+ (negative)[8]

HER2 GENE AMPLIFICATION

NGS, ISH, FISH

- Quantify HER2 gene copies in tissue[3]
- ISH/FISH are recommended to clarify equivocal IHC results (2+)[8]

HER2 GENE MUTATION

NGS

- Identifies HER2-activating mutations in tissue or blood[2]

NGS ALONE MAY OVERLOOK HER2 POSITIVITY IN UP TO 17% OF PATIENTS WITH BILIARY TRACT CANCER[10,11]

*Inclusive of intra- and extrahepatic cholangiocarcinoma.[6]

†Based on a retrospective cohort study.[7]

cfDNA=cell-free DNA; EHR=electronic health record; EMR=electronic medical record; FISH=fluorescence *in situ* hybridization; HER2=human epidermal growth factor receptor 2; IHC=immunohistochemistry; ISH=*in situ* hybridization; NCCN=National Comprehensive Cancer Network®; NGS=next-generation sequencing.

THE PATH TO TARGETED TREATMENT BEGINS BY IDENTIFYING HER2 STATUS[1]

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Testing for HER2 at diagnosis is crucial—it minimizes treatment delay, takes advantage of available tissue, and informs sequencing for targeted approaches like ZIIHERA.[4,12]

TRACK HER2 FROM DIAGNOSIS TO DISEASE PROGRESSION—SO YOU'RE READY TO ACT

CHECK

At diagnosis, test for HER2 with both IHC and NGS; start with IHC when possible[8,9]

CAPTURE

Ensure HER2 and other biomarker results are documented within patient EHR/EMR systems

CONFIRM

Upon progression, recheck patient history for HER2 status; if needed, retest for biomarker status

CHOOSE

Targeted treatment may improve outcomes—if HER2-positive (IHC 3+), choose ZIIHERA, a dual HER2-targeted bispecific antibody[7,13]

DIAGNOSIS

DISEASE PROGRESSION

NCCN

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend testing for HER2 (ERBB2) overexpression and/or amplification in patients with unresectable or metastatic biliary tract cancer to determine if they could benefit from targeted treatment.[2]

WELL-DOCUMENTED TEST RESULTS ARE THE GUIDE TO TARGETED APPROACHES THAT MAY RESULT IN BETTER OUTCOMES[7,8]

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

Please see additional Important Safety Information throughout and full Prescribing Information, including BOXED Warning.

ZIIHERA: THE FDA-APPROVED DUAL HER2-TARGETED BISPECIFIC ANTIBODY FOR ADVANCED HER2+ (IHC 3+) BTC[13]

TEST FOR HER2 TO TAKE ACTION WITH ZIIHERA

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Embryo-Fetal Toxicity (cont'd)

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.

Please see full Prescribing Information, including BOXED Warning.

BTC=biliary tract cancer; FDA=Food and Drug Administration; HER2=human epidermal growth factor receptor 2; IHC=immunohistochemistry.

References: 1. Ayasun R, Ozer M, Sahin I. *Cancers (Basel).* 2023;15(9):2628. **2.** Referenced with permission from The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Biliary Tract Cancers version 2.2025. © 2025 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed July 2, 2025. To view the most recent and complete version of the guidelines, go online to https://www.nccn.org. 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. **3.** Rüschoff J, Hanna W, Bilous M, et al. *Mod Pathol.* 2012;25(5):637-650. **4.** Sepulveda AR, Hamilton SR, Allegra CJ, et al. *J Clin Oncol.* 2017;35(13):1453-1486. **5.** Yu S, Liu Q, Han X, et al. *Exp Hematol Oncol.* 2017;6:31. **6.** Hiraoka N, Nitta H, Ohba A, et al. *Hum Pathol.* 2020;105:9-19. **7.** Lee CH, Seo DH, Fox D, et al. Poster presented at: ASCO Gastrointestinal Cancers Symposium; January 23-25, 2025; California, USA. **8.** Bartley AN, Washington MK, Colasacco C, et al. *J Clin Oncol.* 2017;35(4):446-464. **9.** DiPeri TP, Javle MM, Meric-Bernstam F. *Expert Rev Gastroenterol Hepatol.* 2021;15(5):471-474. **10.** Passaro A, Al Bakir M, Hamilton EG, et al. *Cell.* 2024;187(7):1617-1635. **11.** Nakamura Y, Mizuno N, Sunakawa Y, et al. *J Clin Oncol.* 2023;41(36):5569-5578. **12.** Fox AH, Nishino M, Osarogiagbon RU, et al. *CA Cancer J Clin.* 2023;73(4):358-375. **13.** ZIIHERA (zanidatamab-hrii) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. 2025.

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