EMERGING VIEWPOINTS

ISSUE 01

Featuring

Darshil Shah, MD, MPH, and **Benjamin Weinberg, MD, FACP**

A discussion of unmet need and clinical experience in HER2+ BTC

ADVANCES IN PATIENT CARE

PERSPECTIVES ON THE SECOND-LINE (2L) TREATMENT OF HER2+ BILIARY TRACT CANCER (BTC)

Inside this issue:

- Exploring the challenges of treating advanced BTC following progression
- Highlighting the importance of biomarker testing for patients with BTC
- Discussing treatment options with patients after progression
- Reviewing efficacy, safety, and dosing for a treatment option for advanced HER2+ BTC

A LOOK AT PATIENT CONSIDERATIONS, TESTING, AND TREATMENT STRATEGIES FOR BTC AFTER 1L PROGRESSION

Q. How has the approval of targeted treatment options for BTC over the last 5 years impacted your clinical practice?

Dr. Shah. The introduction of targeted therapies has been a paradigm shift in the 2L treatment landscape of BTC. Cholangiocarcinoma was considered a deadly disease with dismal prognosis. Historically, 2L chemotherapy would only have a ~5% response rate.[1] With 2L targeted therapy, the response rates are much higher,[2-4] and patients live longer with less toxic treatments.[1,5]

Dr. Weinberg. We don't want to miss the opportunity to treat with targeted therapy. Chemotherapy in the 2L setting has limited efficacy and comes with substantial toxicities.[1,2,6] Because we do the biomarker testing, we find more of these potentially actionable targets and we need to make sure we're not missing any, especially for alterations for which treatments are already approved.

Q. From your perspective, what are the biggest challenges in treating advanced BTC in 2L? Given those challenges, what do you consider to be the greatest unmet needs?

Dr. Shah. Key challenges include the limited efficacy of 2L chemotherapy and the prevailing perception that BTC is a death sentence.[1] So, the biggest unmet needs are raising awareness that there are targeted options available and ensuring that biomarker testing is done early—well before progression—and properly documented and recalled as soon as the patient approaches 2L.[7]

Dr. Weinberg. This patient population often has some degree of impaired liver function or other organ dysfunction.[8,9] This limits treatment options in any line setting. As people progress after 1L therapy, they often become more symptomatic, not just from their primary tumor and metastatic disease, but also from treatment toxicity.[8-10] It can become challenging to offer subsequent lines of therapy, especially due to overlapping toxicities from 1L therapy.

Q. What is your current approach to biomarker testing for your patients with BTC?

Dr. Weinberg. If there is tissue available, I generally send for broad molecular testing at diagnosis. That usually encompasses whole exome, whole transcriptome, and pertinent IHC tests to uncover targetable alterations. We often will also send a liquid biopsy. If it hasn't been done in the frontline setting, it really needs to be done prior to 2L. I like testing upfront even though it's unlikely to impact our 1L therapy for advanced BTC. If you don't test, you may not have the information when you're ready for a change. Sometimes, these patients are falling off a cliff. They don't have time to wait 2-4 weeks to get NGS results.

Dr. Shah. We have a big community practice, but we don't have any uniform policy on testing. In my practice, I routinely send both liquid and tissue samples for molecular profiling in all patients with metastatic disease. Additionally, we should be reflex testing all BTC biopsies for HER2 IHC testing.

Q. What factors do you consider when selecting an appropriate 2L therapy for your patient?

Dr. Shah. First and foremost are biomarker testing results. When you have those, you can quickly transition the patient to an appropriate targeted therapy in 2L. I also consider patient fitness and mindset: are they looking to live longer with potentially compromised quality, or are they looking for just good quality of life? Finally, response rate and duration of responses also matter.

Dr. Weinberg. Until we know test results, it's really hard to make an informed decision, especially around 2L therapy. After chemotherapy, patients are often beat up from a neuropathy standpoint rather than from a renal function standpoint. Generally, chemotherapy is associated with more fatigue, nausea, and GI side effects.[8,10] So those definitely factor into the calculus of what drug(s) to use next.

Q. When a patient has progressed following 1L therapy, how do you approach discussing 2L treatment options?

Dr. Weinberg. Often, patients are tired of their 1L therapy even if it's been successful from an efficacy standpoint. The discussion is really around how transitioning to some other therapy will likely be better tolerated, and how they may derive benefit in terms of tumor shrinkage or stabilization, which might help with some of their tumor-related symptoms.

Dr. Shah. It's a tough discussion, especially in BTC. However, when they've been through several months of chemotherapy, they've kind of accepted the diagnosis and prognosis and know the intent is more palliative and focused on quality of life. The nature and severity of toxicities experienced during 1L therapy often inform suitability for 2L treatment. Many patients may not opt for more chemotherapy because quality of life is really important; it's a shared decision-making process.

1L, first line; GI, gastrointestinal; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NGS, next-generation sequencing.

Q. What would you say to a patient or colleague who does not find benefit in continuing therapy following 1L progression?

Dr. Shah. It's essential to assess performance status and align treatment with the patient's goals of care. If you can identify some less toxic treatment options, they'll be more likely to pick those over the chemotherapy-based approaches because quality of life matters. In my experience, for patients with actionable biomarkers, targeted therapy has been a paradigm shift since its side effect profile is generally different from chemotherapy.

Dr. Weinberg. It can be a somewhat dynamic decision based on the day-to-day changes in the patient's functional status and their organ function. Then the bigger question is how they want to spend their time, knowing that they probably have months to live, not years and years. Do they want to spend that time coming and going, not just in and out of the clinic, but in and out of the hospital?

Q. What excites you most about the evolving treatment landscape of HER2+ BTC?

Dr. Shah. That it really gives us an opportunity to offer patients an alternative to chemotherapy or even hospice care; many of these patients will opt for more quality of life and thus forgo further treatment. HER2-targeted therapies can provide durable responses with an acceptable safety profile, giving them another option.[1-4,6]

Dr. Weinberg. The fact that we have approved HER2 options, which is something to be said. We're talking about close to one-third of gallbladder cancers.[11] It's a pretty big chunk of BTCs, which are collectively rare, but still impacts thousands of patients a year. Having any option that's targeted and chemotherapy-free is advantageous for doctors and patients, such that the toxicity profile is generally better than chemotherapy, in my clinical experience.

"It's imperative to make sure that we're doing the appropriate testing and if it's done, we have to make sure it's well documented, accessible, and actionable for the future."
- Dr. Weinberg

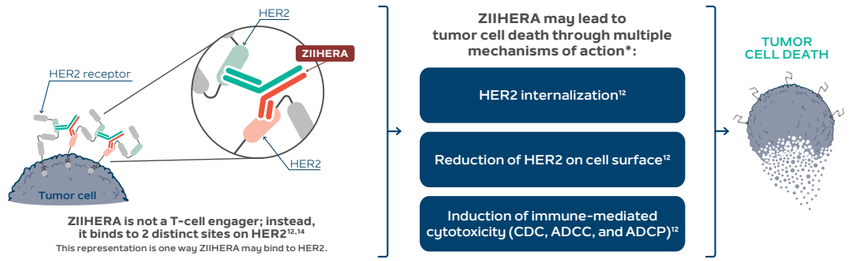
CLINICAL EXPERIENCE: 2L TREATMENT OF ADVANCED HER2+ (IHC 3+) BTC WITH ZIIHERA® (zanidatamab-hrii)

Q. What are the most important things to know about ZIIHERA as a 2L treatment for patients with unresectable or metastatic HER2+ (IHC 3+) BTC?

Dr. Shah. The novel way in which ZIIHERA works and how it can be administered in the community setting. ZIIHERA is a dual HER2-targeted bispecific antibody.[12] Through binding to 2 distinct sites on HER2, ZIIHERA may lead to a reduction of the receptor on the tumor cell surface and induction of complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity, and antibody-dependent cellular phagocytosis.[12,13] Additionally, ZIIHERA is not a bispecific T-cell engager, so we don't expect to be managing adverse events like cytokine release syndrome.[12,14] Overall, ZIIHERA is a truly chemotherapy-free alternative in 2L.

Dr. Weinberg. In my experience, for a previously treated patient with HER2+ (IHC 3+) BTC, I would go with ZIIHERA before other agents. There are other ways to target HER2, but this is a novel mechanism that does not contain a chemotherapy payload[12] and has limited discontinuation and dose reduction due to side effects,[12] in my opinion. There's binding-induced internalization but also some indirect interactions with immune cells, such that you get some degree of inflammatory immune response against the tumor.[12] In my opinion, this is likely driving the prolonged DOR. If it were just targeting one site on HER2, you might see an initial response but not the durability. This leads to favorable responses and tolerability over a longer period of time. The safety profile and the efficacy profile, which are striking in this population, would lead me to use ZIIHERA first in this setting.

ZIIHERA IS A DUAL HER2-TARGETED BISPECIFIC ANTIBODY THAT MAY INDUCE TUMOR CELL DEATH[12]



*These mechanisms result in tumor growth inhibition and cell death *in vitro* and *in vivo*.[12]
ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cell-mediated phagocytosis; CDC, complement-dependent cytotoxicity.

"ZIIHERA is not a bispecific T-cell engager, so we don't expect to be managing adverse events like cytokine release syndrome.[12,14] Overall, ZIIHERA is a truly chemotherapy-free alternative in 2L." **- Dr. Shah**

STUDY DESIGN:

ZIIHERA WAS EVALUATED IN THE LARGEST PHASE 2B CLINICAL TRIAL TO DATE FOR PATIENTS WITH HER2+ BTC.[3,*]

HERIZON-BTC-01 (NCT04466891) is a global, multicenter, single-arm, Phase 2b trial evaluating ZIIHERA in 80 previously treated patients with unresectable or metastatic HER2+ BTC.[3,12] Patients were enrolled into prospectively defined cohorts based on HER2 IHC score.[3] Cohort 1 included 62 patients with HER2 IHC 3+. All 80 patients were included in the safety analyses.[12] Patients received ZIIHERA 20 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity.[12] The primary endpoint was ORR. Select secondary endpoints included DOR, overall survival, progression-free survival, and safety.[3,12] Assessments were performed by ICR per RECIST v1.1.[12]

*Inclusive only of FDA-approved 2L treatments. Current as of 11/2024.[15]

DOR, duration of response; ICR, independent central review; RECIST, Response Evaluation Criteria in Solid Tumors.

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).

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

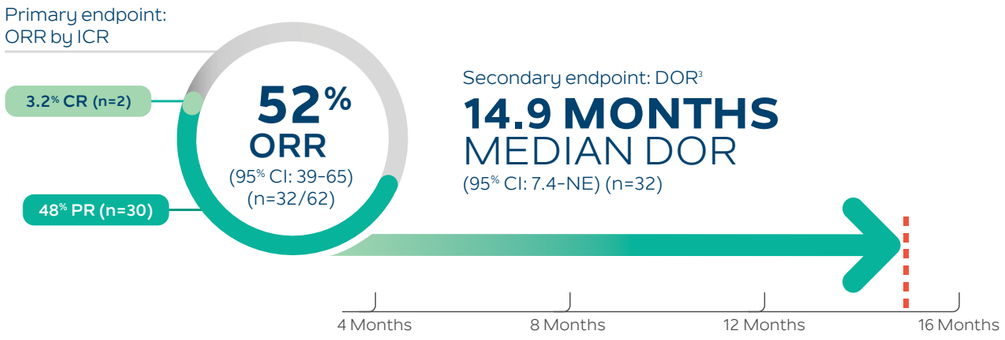
Q. How do the ZIIHERA efficacy data align with your historical expectations for 2L treatment in patients with BTC?

Dr. Shah. When we look at ZIIHERA's 52% ORR and 14.9-month DOR[12]—with the caveat that ZIIHERA and chemotherapy were not compared directly in a 2L head-to-head trial—it's quite remarkable. That is really hard to achieve in 2L metastatic BTC.

Dr. Weinberg. The historical outcomes of this group are unfavorable, but in this biomarker-selected IHC 3+ HER2+ population, you're seeing response rates over 50%.[12] It's not just the response rates but the durability of the response. The median DOR of 14.9 months is very impressive.[12]

"It's not just the response rates but the durability of the response. The median duration of response of 14.9 months is very impressive." **- Dr. Weinberg**

ZIIHERA ACHIEVED COMPELLING AND DURABLE RESPONSES[12]



ZIIHERA DELIVERED ROBUST RESPONSES IN HERIZON-BTC-01[12]

Primary endpoint was ORR per the RECIST v1.1 criteria by ICR. ORR defined as achieving a confirmed best overall response of CR or PR. 95% CIs were based on Clopper-Pearson method. DOR defined as time from the first objective response (CR or PR) that is subsequently confirmed until disease progression or death from any cause; estimates per Kaplan-Meier method, CIs based on the Brookmeyer and Crowley method with log-log transformation. Only patients who had an objective response were included in the DOR analysis.[3]

CI, confidence interval; CR, complete response; NE, not estimable; ORR, objective response rate; PR, partial response.

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.

Please see page 10 for additional Important Safety Information and accompanying full Prescribing Information, including BOXED Warning.

CLINICAL EXPERIENCE: 2L TREATMENT OF ADVANCED HER2+ (IHC 3+) BTC WITH ZIIHERA® (zanidatamab-hrii)

Q. How does the ZIIHERA safety profile impact how you would approach 2L treatment for BTC?

Dr. Weinberg. That these patients can respond for over 1 year with an acceptable safety profile and that very few patients are discontinuing due to adverse events is, in my opinion, quite striking; 2.5% withheld the drug permanently due to adverse events.[12] Very few patients permanently discontinued treatment due to side effects, and 4% required a dose reduction due to an AR.[12] The other thing to highlight is that ZIIHERA does not directly bind to T cells, so some of those concerns that are true for bispecific T-cell engagers are not present.[12,16]

Dr. Shah. In my opinion, acknowledging that there are no head-to-head trials, the side effect profile of any of the alternative regimens—chemotherapy, antibody-drug conjugates, or even other targeted therapies—comes with a substantial set of toxicities.[1,4,5,17] When you look at the ZIIHERA clinical trial, the most common side effects are GI toxicities, like diarrhea, and IRRs.[12] Beyond that, there wasn't any profound immunosuppression or hair loss in the clinical trial for ZIIHERA.[12,14] Also, this is a bispecific antibody that is not a T-cell engager, so it has a distinct safety profile that allows for administration in the outpatient setting.

THE SAFETY PROFILE WAS ESTABLISHED ACROSS 80 PATIENTS IN HERIZON-BTC-01[12]

Adverse Reactions (≥15%)	ZIIHERA (N=80)*	
	All Grades (%)	Grades 3-4 (%)
Gastrointestinal disorders		
Diarrhea†	50	10
Abdominal pain‡	29	1
Nausea	18	1
Vomiting	15	1
Injury, poisoning, and procedural complications		
IRR	35	1
General disorders and administration site conditions		
Fatigue§	24	4
Skin and subcutaneous tissue disorders		
Rash¶	19	0
Metabolism and nutrition disorders		
Decreased appetite	16	0

*Analysis includes 18 patients with HER2 IHC 2+. ARs were graded based on CTCAE v5.0.[12] †Diarrhea includes diarrhea and enteritis.[12] ‡Abdominal pain includes abdominal pain and abdominal pain upper.[12] §Fatigue includes asthenia and fatigue.[12] ¶Rash includes dermatitis, dermatitis acneiform, palmar-plantar erythrodysesthesia syndrome, rash, rash maculo-papular, and rash pustular.[12]

AR, adverse reaction; CTCAE, Common Terminology Criteria for Adverse Events; IRR, infusion-related reaction.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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%.

- Most common ARs (≥20%) are diarrhea, IRR, abdominal pain, and fatigue[12]
- IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.4% of patients[12]
- Most IRRs resolved within 1 day[12]
- Serious ARs occurred in 53% of patients who received ZIIHERA. Those reported 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 AR of hepatic failure occurred in one patient who received ZIIHERA[12]
- There were no reports of cytokine release syndrome[14]
- ARs which resulted in permanent discontinuation in ≥1% of patients who received ZIIHERA included decreased ejection fraction and pneumonitis[12]
- Dosage interruptions due to an AR, excluding temporary interruptions of ZIIHERA infusions due to IRRs, occurred in 41% of patients who received ZIIHERA. Most frequent ARs (>2% of patients) that required dosage interruption were diarrhea, increased alanine aminotransferase, increased aspartate aminotransferase, decreased ejection fraction, pneumonia, cholangitis, fatigue, biliary obstruction, abdominal pain, increased blood creatinine, and decreased potassium[12]
- Dose reductions due to an AR occurred in 4% of patients who received ZIIHERA[12]
- ARs requiring dosage reductions in >1% of patients were diarrhea, nausea, and decreased weight[12]
- 2.5% of patients who received ZIIHERA permanently discontinued treatment due to an AR[12]

LABORATORY ABNORMALITIES THAT WORSENED FROM BASELINE IN PATIENTS RECEIVING ZIIHERA[12]

Laboratory Abnormalities (≥30%)	ZIIHERA (N=80)‖	
	All Grades (%)	Grades 3-4 (%)
Hematology		
Hemoglobin decreased	88	14
Lymphocytes decreased	44	8
Chemistry		
Lactate dehydrogenase increased	55	0
Albumin decreased	53	0
Aspartate aminotransferase increased	47	10
Alanine aminotransferase increased	46	8
Alkaline phosphatase increased	41	5
Sodium decreased	35	10
Potassium decreased	34	5

‖The denominator used to calculate the rate varied from 78 to 80 based on the number of patients with a baseline value and at least one post-treatment value. Analysis includes 18 patients with HER2 IHC 2+.[12]

> "That these patients can respond for over 1 year with an acceptable safety profile and that very few patients are discontinuing due to adverse events is, in my opinion, quite striking."
> **- Dr. Weinberg**

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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.

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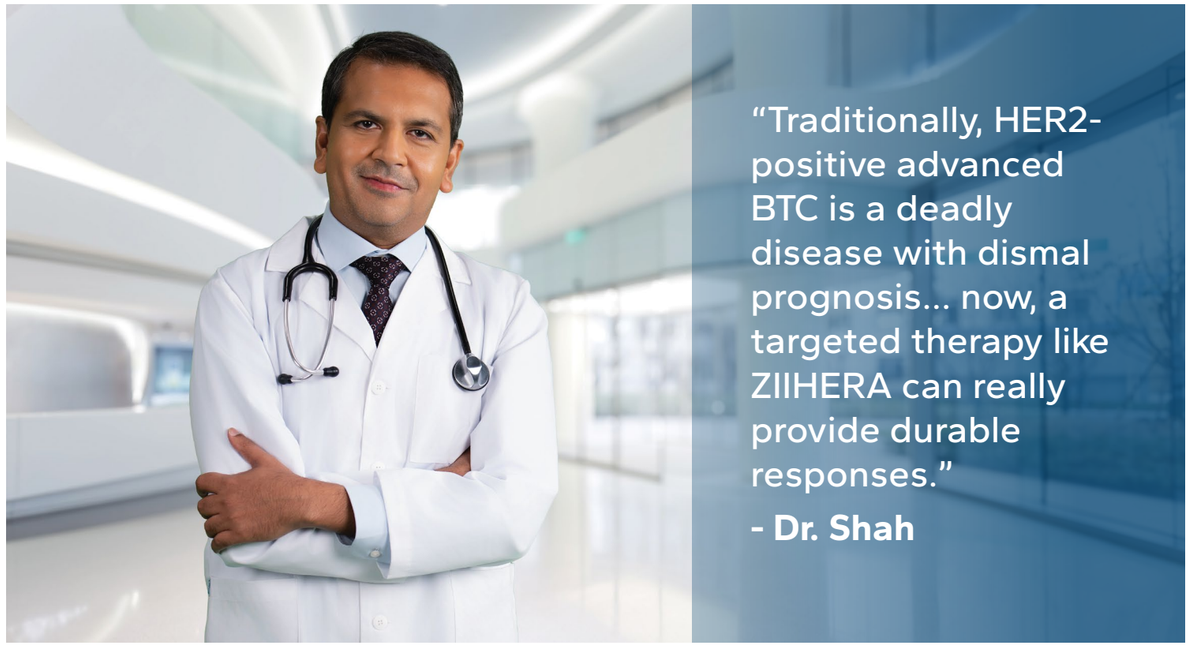
ZIIHERA® (zanidatamab-hrii) 50mg/ml Injection for IV

CLINICAL EXPERIENCE: 2L TREATMENT OF ADVANCED HER2+ (IHC 3+) BTC WITH ZIIHERA® (zanidatamab-hrii)

Q. How do or would you approach discussing ZIIHERA as a treatment option with your patients and colleagues?

Dr. Shah. For both audiences, I would highlight the ORR, DOR, and safety profile of ZIIHERA. For my colleagues, I would also educate them on the importance of performing and properly documenting biomarker testing in all patients with BTC.[7] I would also highlight the dosing schedule of ZIIHERA and what adverse events to monitor both during and after administration.

Dr. Weinberg. With patients, I would say you have a targetable option that is chemotherapy-free and was studied in a very specific population that you are a part of. In my opinion based on the clinical data, you may receive a good response, for not only many months but potentially beyond a year.[12] For my colleagues, I think it's more around the importance of testing every patient. For BTC, there are so many potentially actionable alterations with targetable biomarkers. It's imperative to make sure that we're doing the appropriate testing and if it's done, we have to make sure it's well documented, accessible, and actionable for the future.



"Traditionally, HER2-positive advanced BTC is a deadly disease with dismal prognosis... now, a targeted therapy like ZIIHERA can really provide durable responses."

- Dr. Shah

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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.

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"I would highly recommend broad-based molecular testing. If we're not testing, we're not going to know whether we can use these targeted therapies like ZIIHERA."

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Q. What is your take-home message to healthcare professionals who treat patients with BTC after 1L progression?

Dr. Weinberg. Having any treatment option that's targeted and chemotherapy-free is advantageous for healthcare professionals and patients. I would highly recommend broad-based molecular testing. If we're not testing, we're not going to know whether we can use these targeted therapies like ZIIHERA.

Dr. Shah. Targeted therapy options for BTC have been a paradigm shift. Document the results of biomarker tests, so you remember to act on them as soon as your patient is approaching 2L.[7] It's key to identify HER2+ patients early, so you can switch them to HER2-directed therapy when the time comes.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS

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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%).

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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.

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Please see accompanying full Prescribing Information, including BOXED Warning.

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

"Both the efficacy and safety of ZIIHERA were compelling—impressive response rate, duration of response, and safety profile... this is really a paradigm shift for HER2-positive biliary tract cancers."
- Dr. Shah

Darshil Shah, MD, MPH

Dr. Shah serves as the Director of Gastrointestinal Oncology at Ironwood Cancer & Research Centers in Goodyear, Arizona.

He earned his medical degree at Gujarat University and completed a residency in Internal Medicine at Oakland University William Beaumont School of Medicine. He has a masters in Public Health from the University of Michigan.

Benjamin Weinberg, MD, FACP

Dr. Weinberg is an Associate Professor of Medicine in the Division of Hematology and Oncology at his current institution.

He received his medical degree from the Keck School of Medicine at the University of Southern California. He subsequently completed a residency in Internal Medicine and a fellowship in Hematology and Oncology at MedStar Georgetown University Hospital. He is a member of the American Society of Clinical Oncology.

SCAN OR CLICK HERE to LEARN more about a 2L option for your patients with advanced HER2+ (IHC 3+) BTC at ZIIHERAHCP.com

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.

Please see page 10 for additional Important Safety Information and accompanying full Prescribing Information, including BOXED Warning.

Jazz Pharmaceuticals

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