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ADISINSIGHT REPORT

Zanidatamab: First Approval

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Abstract
Zanidatamab (ZIIHERA®; zanidatamab- hrii), a bi-specific antibody targeting two non-overlapping epitopes of the human epidermal growth factor receptor 2 (HER2) protein, is being developed by Jazz Pharmaceuticals and BeiGene Ltd under license agreements from Zymeworks Inc., the developer of the molecule, for the treatment of HER2-expressing solid tumours. This article summarizes the milestones in the development of zanidatamab leading to this first accelerated approval for use in adults with previously treated, unresectable or metastatic HER2+ (IHC3+) biliary tract cancer (BTC), as detected by an FDA-approved test.

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Zanidatamab (ZIIHERA®): Key Points

A bispecific antibody targeting two different epitopes of the HER2 protein is being developed by Jazz and BeiGene under license agreements from Zymeworks for the treatment of HER2-expressing solid tumours

Received its first approval (under accelerated approval) on 20 November 2024 in the USA

Approved for use in adults with previously treated, unresectable or metastatic HER2+ (IHC3+) BTC, as detected by an FDA-approved test

This profile has been extracted and modified from the *AdisInsight* database. *AdisInsight* tracks drug development worldwide through the entire development process, from discovery, through pre-clinical and clinical studies to market launch and beyond.

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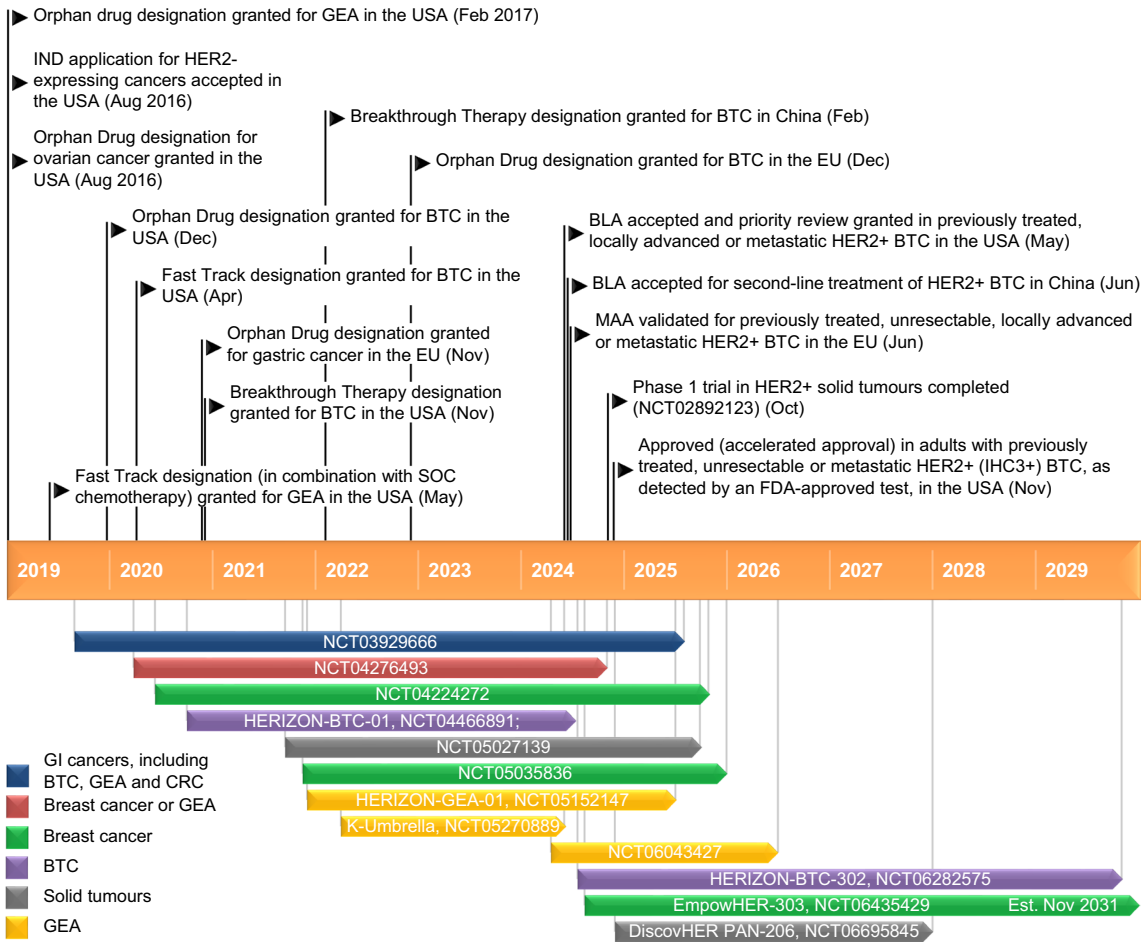
1 Introduction

Human epidermal growth factor receptor 2 (HER2) receptors are overexpressed in a range of solid malignant tumours that often have poor survival rates, including gastrointestinal (GI) cancers, such as gastric/gastroesophageal adenocarcinomas (GEAs) and biliary tract cancer (BTC), and breast cancer. Inhibiting the HER2 pathway is therefore an effective treatment strategy in HER2-expressing cancers [1–3]. Trastuzumab, which targets the juxtamembrane extracellular domain (ECD4), and pertuzumab, which targets the extracellular domain-II (ECD2) and blocks dimerization, were the first two HER2-targeted therapies approved. Both of these monoclonal antibodies and several other HER2-targeting therapies are approved for use in the treatment of HER2+ breast cancer; trastuzumab is the only HER2-targeting therapy approved for use in GEAs. Intrinsic and acquired resistance to HER2-targeting monotherapy remains an issue, and the enhanced anti-tumour activity of trastuzumab and pertuzumab combination therapy seen in HER2-expressing xenograft models is limited to HER2+ breast cancer in a clinical setting [1, 3]. Thus, there is a need for new anti-HER2 therapies with a broader therapeutic range, increased antitumor activity and different mechanisms of action [1, 3, 4].

Zanidatamab (ZIIHERA®; zanidatamab- hrii) is an engineered, bi-specific HER2-directed immunoglobulin G isotype 1 (IgG1)-like antibody developed by Zymeworks Inc., using the Azymetric™ platform [5, 6]. Zanidatamab comprises two unique heavy and light chain pairs that incorporate two different Fab domains to bind to different antigens.



Key milestones in the development of zanidatamab for the treatment of HER2-expressing solid tumours. *BLA* biologics license application, *BTC* biliary tract cancer, *CRC* colorectal cancer, *GI* gastrointestinal, *GEA* gastroesophageal adenocarcinoma, *HER2+* human epidermal growth factor receptor 2 positive, *IND* investigational new drug, *SOC* standard-of-care

Zanidatamab simultaneously targets and binds to two non-overlapping HER2 protein epitopes (ECD4 and ECD2) [3, 7] and is being developed Jazz Pharmaceuticals and BeiGene Ltd for the treatment of HER2-expressing solid tumours [5, 6]. In November 2024, zanidatamab was approved in the USA under accelerated approval based on overall response rate (ORR) and duration of response (DoR) for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC3+) biliary tract cancer (BTC), as detected by an FDA-approved test [7–9]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials [7]. Zanidatamab is also under regulatory review in the EU [10] and in China [11]. Patients eligible for treatment with zanidatamab are selected based on HER2+ (IHC3+) tumour specimens, as detected by an FDA-approved test [7]. The recommended dosage of zanidatamab is 20 mg/kg, administered as an intravenous infusion (IV) once every 2 weeks until disease progression or unacceptable toxicity. To reduce the risk of infusion-related reactions (IRRs), patients should be pre-medicated with paracetamol (acetaminophen), an antihistamine (such as diphenhydramine) and a corticosteroid (such as hydrocortisone) 30–60 min prior to each dose of zanidatamab. The infusion duration for the 1st and 2nd doses is 120–150 mins, reducing to 90 mins for the 3rd and 4th doses if previous infusions are well tolerated, and 60 mins for subsequent doses if previous infusions are well tolerated. If IRRs occur, the infusion should be interrupted, the infusion

rate decreased, and/or treatment permanently discontinued, based on IRR severity [7]. Treatment with zanidatamab can be associated with decreased left ventricular function (LVEF); LVEF should be assessed prior to initiation of treatment and at regular intervals during treatment. If patients develop left ventricular dysfunction (LVD), severe diarrhoea or pneumonitis, treatment should be temporarily withheld or permanently discontinued, based on severity [7]. A reduced zanidatamab dosage (15 mg/kg) may be appropriate for managing some adverse events including diarrhoea and other adverse reactions (excluding LVD, IRR and pneumonitis); if a 15 mg/kg dosage is not tolerated, treatment should be permanently discontinued. There is a boxed warning indicating that exposure to zanidatamab during pregnancy can cause embryo-fetal harm; patients should be advised of the risk and need for effective contraception [7].

1.1 Company Agreements

In October 2022, Jazz Pharmaceuticals and Zymeworks entered an exclusive licensing agreement for the development and commercialization of zanidatamab in the USA, Europe, Japan and all other territories worldwide apart from the Asia/Pacific territories previously licensed to BeiGene, Ltd. [6]. In December 2022, Jazz Pharmaceuticals exercised its option to continue with its exclusive development and commercialisation rights to zanidatamab in the USA, Europe and Japan and all other territories worldwide [12]. In November 2018, BeiGene acquired exclusive rights to develop and commercialize zanidatamab in Asia (excluding Japan), Australia and New Zealand [5].

2 Scientific Summary

2.1 Pharmacodynamics

Zanidatamab binds adjacent HER2 molecules in a *trans* orientation, promoting HER2 receptor crosslinking and initiating distinct HER2 reorganization, evidenced by polarized cell surface HER2 caps and large HER2 clusters [3]. Binding of zanidatamab to HER2 prevents HER2 hetero- and homo-dimerization and intracellular signalling and facilitates HER2 internalisation and subsequent downregulation, leading to a reduction of the HER2 receptor on the tumour cell surface [3, 7]. Zanidatamab also induces complement-dependent cytotoxicity, antibody dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis [3]. These mechanisms of action result in tumour growth inhibition and cell death in vitro and in vivo [3, 7].

The antitumor activity of zanidatamab in patient-derived HER2-expressing xenograft (PDX) models developed from pretreatment or postprogression biopsies in a phase 1 trial in a range of HER2-expressing tumours (NCT02892123) correlated with patient clinical responses. In the postprogression PDX models (all of which were still HER2+), *MET* and *MYC* overexpression/amplification was identified as potential mechanisms of acquired resistance to zanidatamab [13].

2.2 Pharmacokinetics

After the 7th or later dose of IV zanidatamab 20 mg/kg administered every 2 weeks, mean C_{max} is 600 µg/mL, mean C_{trough} is 178 µg/mL, and mean AUC_{336} is 3976 µg·day/mL. With increasing zanidatamab doses, C_{max} is dose proportional and AUC_{∞} is greater than dose proportional. The mean C_{trough} accumulation ratio is ≈ 2.4 [7]. Based on population pharmacokinetic analysis, the mean V_d of zanidatamab is ≈ 7.5 L. Zanidatamab is expected to be metabolized into small peptides by catabolic pathways. Based on population pharmacokinetic analysis, the mean CL of zanidatamab is 0.012 L/h and estimated mean $t_{1/2}$ is ≈ 21 days. Mild and moderate renal impairment (eGFR 30–89 mL/min) and mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN or total bilirubin 1–1.5 times ULN and any AST) had no clinically significant effect on the pharmacokinetics of zanidatamab. The effect of severe renal impairment (eGFR 15–29 mL/min), end-stage renal disease (eGFR < 15 mL/min) with/without haemodialysis, and moderate (total bilirubin > 1.5 to ≤ 3 ULN and any AST) or severe (total bilirubin > 3 ULN and any AST) hepatic impairment on the pharmacokinetics of zanidatamab is unknown [7].

2.3 Therapeutic Trials

2.3.1 Biliary Tract Cancer

Treatment with IV zanidatamab 20 mg/kg every 2 weeks resulted in durable and sustained antitumour activity in patients with unresectable or metastatic HER2+ (IHC3+ or IHC2+ by central assessment; cohort 1) BTC in the phase 2b HERIZON-BTC-01 (NCT04466891) trial [7, 14, 15]. In the cohort 1 ($n = 80$), confirmed ORR (cORR; primary endpoint) was 41.3% (2 CR, 31 PR), and in the subgroup of patients with IHC3+ tumours ($n = 62$), cORR was 52% (2 CR, 30 PR) [median duration of follow-up 21.9 months] [7, 15]. In patients with IHC3+ tumours, median DoR was 14.9 months, DoR ≥ 6 months was 59% and DoR ≥ 12 months was 44% [7]. Median progression-free survival (PFS) was 7.2 months, 12-month overall survival (OS) probability was 65.0% and median OS was 18.1 months [15]. Eligible

Features and properties of zanidatamab

Alternative names	JZP-598; ZW 25; Zanidatamab-hrii; Ziihera
Class	Antineoplastics; bispecific antibodies; immunotherapies
Mechanism of action	Antibody-dependent cell cytotoxicity; phagocyte stimulants
Route of administration	IV
Pharmacodynamics	Binds to two non-overlapping HER2 protein epitopes (ECD4 and ECD2) Binds adjacent HER2 molecules in a *trans* orientation, promoting HER2 receptor crosslinking and initiating distinct HER2 reorganization; prevents HER2 hetero- and homo-dimerization and intracellular signalling; facilitates HER2 internalisation and subsequent downregulation, reducing HER2 receptors on cell surface; induces CDC, ADCC and ADCP
Pharmacokinetics	C_{max} 600 μg/mL, C_{trough} 178 μg/mL, AUC_{336} 3976 μg·day/mL, C_{trough} accumulation ratio ≈ 2.4, V_d ≈ 7.5 L, CL 0.012 L/h, $t_{1/2}$ ≈ 21 days
Adverse reactions	
Most frequent	Diarrhoea, IRR, abdominal pain, fatigue, rash, nausea, decreased appetite, vomiting
Serious	Biliary obstruction, biliary tract infection, sepsis, pneumonia, diarrhoea, gastric obstruction, fatigue, liver failure
Occasional	Left ventricular dysfunction, pneumonitis
ATC codes	
WHO ATC code	L01F-D07 (Zanidatamab)
EphMRA ATC code	L1X (all other antineoplastics)

patients had received ≥ 1 prior gemcitabine-containing systemic chemotherapy regimen in the advanced disease setting and had adequate cardiac function (LVEF ≥ 50%). Zanidatamab was administered until disease progression or unacceptable toxicity. ORR and DoR were determined by an independent central review. All patients had received ≥ 1 prior line of gemcitabine-based therapy, 31% had received 2 prior lines of therapy, and 10% had received ≥ 3 prior lines of therapy for unresectable or metastatic disease [7, 14].

2.3.2 Other Gastrointestinal Cancers

In the GEA subgroup of a phase 2 trial of first-line zanidatamab every 3 weeks plus chemotherapy in patients with HER2+ (IHC3+ or IHC2+/FISH+) GI cancers (NCT03929666) [16] at a median 41.5 months' follow-up, cORR was 84% (4 CR, 27 PR; $n = 37$ evaluable patients with centrally confirmed HER2+ GEA), median DoR was 18.7 months and median PFS was 15.2 months. The Kaplan-Meier estimated 30-month OS probability was 59%. Patients received zanidatamab 30 mg/kg, 1800 mg (patients < 70 kg) or 2400 mg (patients ≥ 70 kg) every 3 weeks plus standard combination chemotherapy [16].

In the cohort of patients with advanced HER2+ GEA who received 1st line therapy with zanidatamab plus chemotherapy and tislelizumab in a phase 1b/2 trial (NCT04276493) [17], at a median 18.2 months' follow-up, cORR was 75.8% (1 CR and 24 PR; $n = 33$ evaluable), median DoR was 22.8 months and median PFS was 16.7 months [17].

In the colorectal subgroup of a phase 2 trial of first-line zanidatamab plus chemotherapy ± bevacizumab in patients with HER2+ (IHC3+/FISH+ or IHC2+/FISH+) GI cancers (NCT03929666) [18], at a median 15.4 months' follow-up, cORR was 90.9% (10 PR; $n = 11$ evaluable patients), and median DoR and median PFS were not reached. Patients received zanidatamab 1200 mg (patients < 70 kg) or 1600 mg (patients ≥ 70 kg) every 2 weeks plus physician's choice of chemotherapy ± bevacizumab [18].

2.3.3 Breast Cancer

In a phase 2a trial of zanidatamab 20 mg/kg every 2 weeks plus palbociclib and fulvestrant in unresectable, locally advanced or metastatic HER2+/HR+ metastatic breast cancer (NCT04224272) [19], PFS at 6 months (PFS6; primary endpoint) at a median follow-up of 16.1 months was 67% ($n = 51$ evaluable), median PFS was 11.7 months and cORR was 34.8% (3 CR and 13 PR). The median DoR was 14.8 months [19].

In the cohort of patients with advanced HER2+ breast cancer who received 1st line therapy with zanidatamab 30 mg/kg or 1800 mg plus docetaxel every 3 weeks in a phase 1b/2 trial in China, Korea and Taiwan (NCT04276493) [20], the cORR was 90.9% (2 CR and 28 PR; $n = 33$ evaluable) at a median follow-up of 15.5 months and the median DoR was not reached [20].

In a phase 1 trial in patients with locally advanced and/or metastatic HER2+ (IHC3+ or IHC2+/FISH+) breast cancer who had previously received HER2-targeted therapy

(NCT02892123), treatment with zanidatamab plus chemotherapy achieved a cORR of 37.5% ($n = 16$ evaluable); median DoR was not reached [21].

A pathologic complete response with no residual cancer burden (RCB-0) was achieved in 6 of 20 patients following neoadjuvant therapy with 6–10 doses of zanidatamab 20 mg/kg on days 1 and 15 of a 28-day cycle in a phase 2 trial in node negative stage 1 HER2+ (IHC3+ or IHC2+/ISH+) breast cancer (NCT05035836) [22]. A further 4 patients had RCB-1, 9 patients had RCB-2 and 1 patient had RBC-3 [22]. Patients with HER2+ ER+ breast cancer also received endocrine therapy from day 1 of cycle 1 [22].

The combination of zanidatamab with evorpacept (a high-affinity CD47-blocking fusion protein) showed promising antitumour activity in a cohort of heavily pretreated patients with HER2+ metastatic breast cancer in a phase 1b/2 trial (NCT05027139) [23]. At the recommended dose [zanidatamab 1200 mg (patients < 70 kg) or 1600 mg (pts ≥ 70 kg) + evorpacept 30 mg/kg IV every 2 weeks] in patients with centrally confirmed HER2+ tumours (9/21 patients with locally assessed HER2+ tumours), the cORR was 55.6% (5 PR), median DoR was not reached and median PFS was 7.4 months. In the 12 patients who were not confirmed as HER2+ by central assessment, cORR was 16.7% (2 PR), median DoR was not reached and median PFS was 3.5 months. In the cohort of patients with HER2-low metastatic breast cancer (IHC1+ or IHC2+/ISH negative; n = 15), the cORR was 20% (3 PR), median DoR was 5.5 months and median PFS was 1.9 months [23].

2.3.4 Other Cancers

In a phase 1 dose-escalation and dose expansion study in patients with treatment refractory locally advanced or metastatic HER2-expressing or *HER2*-amplified cancers (NCT02892123), in the dose expansion part 2 of the trial (in patients with any cancers other than breast cancer or gastroesophageal) where patients received IV zanidatamab 20 mg/kg every 2 weeks, the cORR was 37% (31/83 evaluable patients; all PR). Median DoR was 6.9 months and median PFS was 5.4 months. Most tumours in the 86 patients enrolled in part 2 were HER2+ IHC3+ (73%) or IHC2+ (26%) [4].

In a phase 1 dose-escalation trial of zanidatamab in Japanese patients with treatment-refractory metastatic or unresectable HER2-expressing tumours (jRCT2031210161) [24], cORR at data cut-off ($n = 25$ evaluable patients; median of 3.5 cycles) was 20% and one patient with gallbladder cancer achieved CR. Median DoR was not evaluable and median PFS was 3.7 months. Zanidatamab was administered at 20 mg/kg every 2 weeks ($n = 7$), 30 mg/kg every 3 weeks (n = 9), or 1800 mg every 3 weeks ($n = 12$). Patient tumours were HER2+ IHC1+ ($n = 10$), IHC2+ ($n = 9$) or IHC3+ (n = 9) [24].

2.4 Adverse Events

The most common adverse reactions (incidence ≥ 15%) in patients with BTC treated with IV zanidatamab 20 mg/kg monotherapy every 2 weeks in the phase 2 HERIZON-BTC-01 trial were diarrhoea [50% (all grades); 10% (grade 3/4)], IRR (35%; 1%), abdominal pain (29%; 1%), fatigue (24%; 4%), rash (19%; 0%), nausea (18%; 1%) decreased appetite (16%; 0%) and vomiting (15%; 1%). The most frequent laboratory abnormalities (incidence ≥ 30%) were decreased haemoglobin (88%; 14%), increased lactate dehydrogenase (55%; 0%), decreased albumin (53%; 0%), increased AST (47%; 10%), increased ALT (46%; 8%), decreased lymphocytes (44%; 8%), increased alkaline phosphatase (41%; 5%), decreased sodium (35%; 10%) and decreased potassium (34% vs 5%). Serious adverse reactions occurred in 53% of patients, the most frequent being biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhoea (3.8%), gastric obstruction (3.8%) and fatigue (2.5%). One fatal reaction (liver failure) occurred [7]. Dosage interruptions because of adverse reactions (excluding those due to IRRs) occurred in 41% of patients, and the most common of these (incidence > 2%) were diarrhoea, increased ALT, increased AST, decreased LEVF, pneumonia, cholangitis, fatigue, biliary obstruction, abdominal pain, increased blood creatinine, and decreased potassium. Dosage reductions due to an adverse reaction occurred in 4% of patients and these included diarrhoea, nausea and decreased weight. 2.5% of patients permanently discontinued zanidatamab treatment because of adverse reactions (these included decreased LEVF and pneumonitis) [7].

Among adverse reactions of interest reported in patients ($n = 233$) administered zanidatamab 20 mg/kg monotherapy in two clinical trials (phase 1 NCT02892123 and phase 2 NCT04466891), LVEF declined by > 10% and decreased to < 50% in 4.3% of patients. LVD resolved in 70% of patients and led to permanent discontinuation of zanidatamab in 0.9% of patients. The median time to first occurrence of LVD was 5.6 months. Diarrhoea was reported in 48% of 233 patients (25% grade 1, 17% grade 2, 6% grade 3). An IRR was reported in 31% of 233 patients (5.6% grade 1, 25% grade 2, 0.4% grade 3); permanent treatment discontinuation due to IRRs occurred in 0.4% of patients. IRRs occurred on the first day of dosing in 28% of patients and 97% of IRRs resolved within 1 day [7].

Key clinical trials of zanidatamab

Drug(s)	Indication	Phase	Status	Location(s)	Sponsor/collaborator	Identifier
Zanidatamab, gemcitabine, cisplatin, pembrolizumab durvalumab	HER2+ BTC	3	Recruiting	Global	Jazz Pharmaceuticals	NCT06282575; HERIZON-BTC-302
Zanidatamab, tislelizumab, trastuzumab, capecitabine, oxaliplatin/cisplatin, 5-FU	HER2+ GEA	3	Recruiting	Global	Jazz Pharmaceuticals, BeiGene, Ltd	NCT05152147; HERIZON-GEA-01; EudraCT2021-000296-36
Zanidatamab, trastuzumab, eribulin, vinorelbine, gemcitabine, capecitabine	HER2+ breast cancer	3	Recruiting	USA	Jazz Pharmaceuticals	NCT06435429; EmpowHER-303
Zanidatamab	HER2+ BTC	2b	Completed	Global	Jazz Pharmaceuticals, BeiGene, Ltd	NCT04466891; HERIZON-BTC-01; EudraCT2020-000459-11
Zanidatamab, capecitabine, oxaliplatin/cisplatin, fluorouracil, leucovorin, bevacizumab, gemcitabine	HER2+ gastrointestinal cancers (including BTC, GEA, CRC)	2	Ongoing	USA, Canada, Chile, Korea	Jazz Pharmaceuticals	NCT03929666
Zanidatamab, palbociclib, fulvestrant	HER2+/HR+ breast cancer	2	Ongoing	USA, Canada Spain	Jazz Pharmaceuticals	NCT04224272; EudraCT2019-002956-18
Zanidatamab, letrozole, tamoxifen	HER2+ breast cancer	2	Ongoing	USA	M. D. Anderson Cancer Center, Zymeworks	NCT05035836
Zanidatamab, ramucirumab, paclitaxel	HER2+ GEA	2	Recruiting	Canada	Canadian Cancer Trials Group, Jazz Pharmaceuticals	NCT06043427
Zanidatamab, tislelizumab	HER2+ GEA	2	Completed	Korea	Yonsei University	NCT05270889; K-Umbrella
Zanidatamab, tislelizumab, docetaxel, capecitabine, oxaliplatin	HER2+ breast cancer or GEA	1b/2	Completed	China, Korea, Taiwan	BeiGene, Ltd	NCT04276493; CTR20210237
Zanidatamab	HER2+ (IHC3+) solid tumours	2	Recruiting	USA	Jazz Pharmaceuticals	NCT06695845; DiscovHER PAN-206
Zanidatamab, evorpacept	HER2+ solid tumours	1b/2	Ongoing	USA	Jazz Pharmaceuticals, ALX Oncology Inc.	NCT05027139
Zanidatamab	HER2+ solid tumours	1	Ongoing	Japan	Jazz Pharmaceuticals	jRCT2031210161

BTC biliary tract cancer, *CRC* colorectal cancer, *GEA* gastroesophageal adenocarcinoma

2.5 Companion Diagnostic

On 20 November 2024, a label expansion for the PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody test to include BTC and aid in identifying patients with HER2+ BTC who are eligible for treatment with zanidatamab was approved in the USA [8, 25].

2.6 Ongoing Clinical Trials

Three phase 3 trials of zanidatamab are recruiting: the HERIZON-BTC-302 trial (NCT06282575) evaluating zanidatamab plus standard chemotherapy ± a programmed cell death protein-1/ligand 1 (PD-1/L1) inhibitor (pembrolizumab or durvalumab at physician's discretion if locally approved) in advanced/metastatic HER2+ BTC [26], the HERIZON-GEA-01 trial (NCT05152147) evaluating zanidatamab plus standard chemotherapy with/without tislelizumab in advanced/metastatic HER2+ GEA [27] and the Empow-HER-303 trial (NCT06435429) comparing zanidatatmab plus standard chemotherapy versus trastuzumab plus standard chemotherapy in patients with metastatic HER2+ breast cancer who have progressed on/are intolerant to trastuzumab deruxtecan [28]. Phase 2 trials of zanidatamab in HER2+ GEA (NCT06043427) and HER2+ (IHC3+) solid tumours (NCT06695845; DiscovHER PAN-206) are also recruiting.

Active zanidatamab trials no longer recruiting include phase 2 trials in HER2+ GI cancers (NCT03929666), HER2+/HR+ breast cancer (NCT04224272), and HER2+ breast cancer (NCT05035836); a phase 1b/2 trial in combination with evorpacept in HER2+ solid tumours (NCT05027139); and a phase 1 Japanese trial in HER2+ solid tumours (jRCT2031210161).

Zanidatamab is included among the targeted therapies being evaluated in the international phase 3 SAFIR-ABC10 platform study (NCTT05615818), which is investigating whether introducing targeted therapy after 4 cycles of current first-line SOC treatment for advanced BTC improves efficacy. Zanidatamab is also included in the PRE-I-SPY oncology platform program in the neoadjuvant setting [29] and is being evaluated in HER2+ breast cancer in a phase 1 trial in combination with tucatinib (NCT05868226; PRE-I-SPY-P1/I-SPY-P1) and a phase 2 trial as monotherapy followed by standard-of-care (NCT01042379; I-SPY-2).

3 Current Status

Zanidatamab received its first approval on 20 November 2024 (accelerated approval) for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC3+) BTC, as detected by an FDA-approved test in the USA [7]. Zanidatamab is also under regulatory review in the EU [10] and in China [11].

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Declarations

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Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability Not applicable.

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