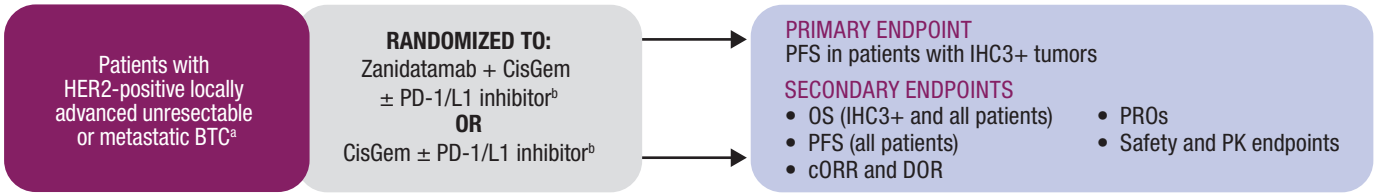
A Phase 3, Global, Open-Label, Randomized Trial of the Efficacy and Safety of Zanidatamab With Standard-of-Care Therapy Against Standard-of-Care Therapy Alone for Advanced HER2-Positive Biliary Tract Cancer (HERIZON-BTC-302) – (NCT06282575)

Study Overview



[a]HER2-positive disease defined as IHC3+ or IHC2+/ISH+ by central testing.
[b]Physician's choice of either durvalumab or pembrolizumab, where approved under local regulations.

Purpose	To evaluate the efficacy and safety of zanidatamab plus CisGem with or without a PD-1/L1 inhibitor (physician's choice of either durvalumab or pembrolizumab, where approved under local regulations) as first line of treatment for patients with HER2-positive BTC
Condition(s)	HER2-positive BTC
Drug(s)	• Zanidatamab • Cisplatin • Gemcitabine • Pembrolizumab • Durvalumab
Study Phase	Phase 3
Participating Countries (Active and Planned)	Global[c]

[c]Sites outside the United States are not yet open.

Selected Outcome Measures

Primary Outcome Measure:

- PFS in patients with IHC3+ tumors

Secondary Outcome Measures:

- OS in patients with IHC3+ tumors
- PFS in all patients
- OS in all patients
- Number of patients achieving cORR
- DOR
- Number of patients reporting TEAEs
- Maximum serum concentration of zanidatamab
- Number of patients who develop ADAs to zanidatamab
- TDD for patients with IHC3+ tumors in patient-reported PF domain score as measured by EORTC QLQ-C30
- TDD for all patients in patient-reported PF domain score as measured by EORTC QLQ-C30
- TDD for patients with IHC3+ tumors in patient-reported symptoms scores as measured by EORTC QLQ-BIL21 (pain, jaundice, abdominal pain, pruritus)
- TDD for all patients in patient-reported symptoms scores as measured by EORTC QLQ-BIL21 (pain, jaundice, abdominal pain, pruritus)

Contact information:

ClinicalTrialDisclosure@JazzPharma.com

http://www.clinicaltrials.gov
(Identifier: NCT06282575)

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Key Eligibility Criteria

Key Inclusion Criteria:

- Histologically or cytologically confirmed BTC, including GBC, ICC, or ECC
- Locally advanced unresectable or metastatic BTC and not eligible for curative resection, transplantation, or ablative therapies
- Receipt of ⩽2 cycles of systemic therapy with gemcitabine and a platinum agent with or without a PD-1/L1 inhibitor (physician's choice of durvalumab or pembrolizumab, where approved under local regulations) for advanced unresectable or metastatic disease
- HER2-positive disease (defined as IHC3+; or IHC2+/ ISH+) by IHC and ISH assays (in patients with IHC2+ tumors) at a central laboratory on new biopsy tissue or archival tissue from the most recent biopsy
- Assessable (measurable or non-measurable) disease as defined by RECIST v1.1 per investigator assessment
- ⩾18 years of age (or the legal age of adulthood per country-specific regulations)
- ECOG performance status of ⩽1
- Adequate organ function
- Females of childbearing potential must have a negative pregnancy test result
- Females of childbearing potential and males with a partner of childbearing potential must be willing to use two methods of birth control

Key Exclusion Criteria:

- Prior treatment with a HER2-targeted agent
- Prior treatment with checkpoint inhibitors, other than durvalumab or pembrolizumab
- Patients with the following BTC histologic subtypes: small cell cancer, neuroendocrine tumors, lymphoma, sarcoma, mixed tumor histology, and mucinous cystic neoplasms detected in the biliary tract region
- Use of systemic corticosteroids
- Brain metastases
- Severe chronic or active infections
- History of allogeneic organ transplantation
- Active or prior autoimmune inflammatory conditions
- History of interstitial lung disease or non-infectious pneumonitis
- Participation in another clinical trial with an investigational medicinal product within the last 3 months
- Females who are breast feeding
- Any other medical, social, or psychosocial factors that, in the opinion of the investigator, could impact safety or compliance with study procedures

Treatment Regimen

- **Experimental (zanidatamab with SOC):** Zanidatamab and CisGem with or without pembrolizumab or durvalumab
- **Active comparator (SOC):** CisGem with or without pembrolizumab or durvalumab

ADA = anti-drug antibodies, BTC = biliary tract cancer, CisGem = cisplatin and gemcitabine, cORR = confirmed objective response rate, DOR = duration of response, ECC = extrahepatic cholangiocarcinoma, ECOG = Eastern Cooperative Oncology Group, EORTC = European Organisation for Research and Treatment of Cancer, GBC = gallbladder cancer, HER2 = human epidermal growth factor receptor 2, ICC = intrahepatic cholangiocarcinoma, IHC = immunohistochemistry, ISH = in situ hybridization, OS = overall survival, PD-1/L1 = programmed cell death-protein 1/ligand 1, PK = pharmacokinetics, PF = physical functioning, PFS = progression-free survival, PRO = patient-reported outcome, QLQ-BIL21 = Quality of Life Questionnaire Cholangiocarcinoma and Gallbladder Cancer Module, QLQ-C30 = Quality of Life Questionnaire Core 30, RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1, SOC = standard of care, TDD = time to definitive deterioration, TEAE = treatment-emergent adverse event.

Jazz Pharmaceuticals