PROTOCOL CONTAINS BISPECIFIC THERAPY	
Indication	Monotherapy treatment for HER2-positive locally advanced or metastatic biliary tract cancer after 1 or more lines of systemic treatment.
Treatment Intent	Palliative.
Frequency and number of cycles	Repeat every 14 days Continue until disease progression, unacceptable toxicity or patient's choice.

Monitoring Parameters	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion.
	• **FBC, U&Es** and **LFTs** at each cycle.
	• If neuts <1 and platelets <75 discuss with consultant.
	• **Hepatic impairment:** no recommended dose adjustment in mild impairment (total bilirubin </=ULN and AST > ULN or total bilirubin between 1 and 1.5 times ULN and any AST). Zanidatamab has not been evaluated in patients with moderate to severe impairment. As there is minor involvement of hepatic processes in the clearance of zanidatamab, no dose adjustment is recommended for patients with hepatic impairment as no difference in exposure is expected.
	• **Renal impairment:** no dose adjustment required in mild or moderate impairment (CrCl 30-89ml/min) zanidatamab has not been evaluated in patients with severe renal impairment and patients with end-stage renal disease with or without dialysis. As there is minor involvement of renal processes in the clearance of zanidatamab, no dose adjustment is recommended for patients with renal impairment as no difference in exposure is expected.
	• **ECHO** at baseline pre-cycle 1, pre-cycle 3, then every 12 weeks throughout treatment. Patients with a baseline left ventricular ejection fraction (LVEF) value of <50%, a history of clinically significant cardiac events or disease should be treated at the clinician's discretion due to no data in patients with cardiac disease (such as history of myocardial infarction, unstable angina, ventricular arrhythmia requiring therapy, uncontrolled hypertension, or any history of symptomatic congestive heart failure).
	• **Management of adverse reactions and dose adjustments:**
	  ○ **Infusion-related reactions:** Patients should be monitored for signs and symptoms of IRRs during administration and as clinically indicated after completion of infusion. Management of IRRs may require reduced infusion rate, dose interruption, or treatment discontinuation see Table 2.
	  ○ **LVEF dysfunction**: In the event of a decrease in ventricular ejection fraction (LVEF) dose delay may be required, see table 1.
	  ○ **Pneumonitis:** Patients should be monitored for signs and symptoms of pneumonitis. In the event of confirmed >/= Grade 2 pneumonitis, treatment should be permanently discontinued.
	• **Common drug interactions (for comprehensive list refer to BNF/SPC):** no formal drug studies have been performed.
	• **Missed dose:** If a dose is missed, the scheduled dose should be administered as soon as possible. The administration schedule should be adjusted to maintain a 2-week interval between doses.
	• **Driving and machinery:** Zanidatamab may cause fatigue, patients should be advised to use caution when driving or operating machines.
	• **Pregnancy and contraception:** Patients should be advised to avoid becoming pregnant during treatment and use an effective method of contraception while receiving zanidatamab and for 4 months following the last dose.
	• This medicinal product contains polysorbate which may cause allergic reactions.

References	SPC accessed online 24.04.2026 CDF list V1.394 accessed online 26.04.2026 https://clinicaltrials.gov/study/NCT04466891 https://pmc.ncbi.nlm.nih.gov/articles/instance/12635922/bin/jamaoncol-e254736-s001.pdf

NB for funding information, refer to CDF and NICE Drugs Funding List

Table 1. Dose modifications for left ventricular dysfunction

Left ventricular dysfunction	**Severity**	**Treatment modification**
	Absolute decrease of ≥ 16% points in LVEF from pre-treatment baseline	• Withhold treatment for at least 4 weeks. • Repeat LVEF assessment within 4 weeks. • Resume treatment within 4 to 8 weeks, if LVEF returns to normal limits and the absolute decrease is ≤ 15% points from baseline. • If LVEF has not recovered to within 15% points from baseline, permanently discontinue.
	LVEF value below 50% and absolute decrease of ≥ 10% points below pre-treatment baseline	

Table 2. Dose and infusion duration modifications for infusion-related reactions

Infusion related reactions	**Severity**	**Treatment modification**
	Mild (Grade 1)	• Reduce infusion rate by 50%. • Subsequent infusions should start at this reduced rate. • Infusion rate for subsequent infusions may be increased gradually to the rate prior to symptoms, as tolerated.
	Moderate (Grade 2)	• Hold infusion immediately. • Treat with appropriate therapy. • Resume infusion at 50% of previous infusion rate once symptoms resolve. • Infusion rate for subsequent infusions may be increased gradually to the rate prior to symptoms, as tolerated.
	Severe (Grade 3)	• Hold infusion immediately. • Promptly treat with appropriate therapy. • Resume infusion at the next scheduled dose at 50% of previous infusion rate once symptoms resolve. • Permanently discontinue for recurrent Grade 3 symptoms.
	Life threatening (Grade 4)	• Hold infusion immediately. • Promptly treat with appropriate therapy. • Permanently discontinue.

Repeat every 14 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone	10mg	IV	stat	Given 30-60minutes prior to the zanidatamab injection.
	Paracetamol	1g	PO	stat	
	Chlorphenamine	4mg	PO	stat	
	Metoclopramide	20mg	PO	stat	
	ZANIDATAMAB	**20mg/kg**	IV	*see below	In 500ml sodium chloride 0.9% with 0.22micron in-line PES filter The final concentration of the diluted solution should be between 0.4 mg/mL and 6 mg/mL
	* **1st** and **2nd** dose administer over 120-150 minutes, **3rd** and **4th** dose if previous dose tolerated administer over 90 minutes, **5th** dose onwards if previous dose tolerated administer over 60 minutes				

TTO	Drug	Dose	Route	Directions
Day 1	Loperamide	2mg-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on Cycle 1 then only if required.
	Metoclopramide	10mg	PO	Take 10mg up to 3 times a day as required (max. 30mg per day including 20mg pre-med dose). Do not take for more than 5 days continuously. Dispense on Cycle 1 then only if required.