Zanidatamab

Indication

Unresectable locally advanced or metastatic HER2-positive (IHC3+) biliary tract cancer after 1 or more lines of systemic treatment.

Regimen details

Zanidatamab 20mg/Kg by intravenous infusion

Cycle frequency

Every 14 days

Number of cycles

Continue treatment until disease progression or unacceptable toxicity

Administration

Zanidatamab is given in 500mls sodium chloride 0.9% via a 0.2 or 0.22 micron polyethersulfone (PES) in-line filter.

Infusion times are as follows:
First and second infusions are given over 2 hours,
If well-tolerated, the third and fourth infusions can be given over 90 minutes, and subsequent infusions can be given over 60 minutes.

Infusion-related reactions/ hypersensitivity

Management of infusion related reactions (IRRs) may require reduced infusion rate, dose interruption, or treatment discontinuation as described below.

Dose and infusion duration modifications for infusion-related reactions

Infusion related reactions (see sections 4.4 and 4.8)	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.

Pre-medication

Premedication should be administered 30 to 60 minutes prior to each infusion to prevent potential infusion related reactions.

Paracetamol 1000mg PO
Chlorphenamine 10mg IV
Dexamethasone 10mg IV

Emetogenicity

Minimal

Additional supportive medication

None

Extravasation

Neutral

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Echocardiogram or MUGA (LVEF)	3 months

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)

Medical review every 4 weeks initially

Left ventricular function must be assessed at baseline and at regular intervals during treatment.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.5 x 10^9/L
Platelet count	≥ 75 x 10^9/L
Haemoglobin	≥ 90g/L
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN (or ≤3 x ULN for patients with Gilbert's disease)
AST	< 3 x ULN (or <5 x ULN if liver involvement)
ALT	< 3 x ULN (or <5 x ULN if liver involvement)
LVEF	>50%

Dose modifications

Dose modifications for left ventricular dysfunction

Left ventricular dysfunction (see section 4.4)	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	

Dose modifications for pneumonitis

Pneumonitis (see section 4.4)	Severity	Treatment modification
	Confirmed Grade ≥ 2	• Permanently discontinue.

Renal impairment - Dose adjustments are not required for patients with mild or moderate renal impairment (eGFR 30 to 89 mL/min. Zanidatamab has not been evaluated in patients with severe renal impairment and patients with end-stage renal disease with or without dialysis. However, due to 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

Hepatic impairment - Dose adjustments are not required for patients with mild hepatic impairment (total bilirubin ≤ upper limit of normal (ULN) and aspartate aminotransferase (AST) > ULN or total bilirubin between 1 and 1.5 times ULN and any AST). Zanidatamab has not been evaluated in patients with moderate (total bilirubin > 1.5 to ≤ 3 ULN and any AST) to severe (total bilirubin > 3 ULN and any AST) hepatic impairment. However, due to 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

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Left ventricular dysfunction*
Pneumonitis**

- **Frequently occurring side effects**

Diarrhoea
Fatigue
Anaemia
Rash
ALT and AST increases
Nausea/vomiting
Decreased appetite

- **Other side effects**

Infusion reactions

***Left ventricular dysfunction**
Decreases in LVEF have been reported with medicinal products that block HER2 activity, including

zanidatamab. LVEF should be assessed prior to initiation of zanidatamab by echocardiogram or multigated acquisition (MUGA) scan and at regular intervals during treatment to ensure that LVEF is within normal limits. If the LVEF declines and has not improved, or has declined further at the subsequent assessment, zanidatamab should be discontinued as recommended above.
Zanidatamab has not been studied in patients with a pre-treatment LVEF value of < 50%; history of myocardial infarction or unstable angina within 6 months; troponin levels consistent with myocardial infarction, or clinically significant cardiac disease such as ventricular arrhythmia requiring therapy, uncontrolled hypertension, or any history of symptomatic congestive heart failure (CHF).
****Pneumonitis**
Pneumonitis has been reported with medicinal products that block HER2 activity, including zanidatamab. Pneumonitis has been reported in 0.4% of 233 patients treated with Zanidatamab 20 mg/kg intravenously as a single agent in clinical studies. Patients should be monitored for signs and symptoms of pneumonitis. In the event of confirmed Grade ≥ 2 pneumonitis, treatment should be permanently discontinued as above.

Significant drug interactions – for full details consult product literature/ reference texts

No dedicated clinical studies evaluating the drug interaction potential of zanidatamab have been conducted. Zanidatamab is an antibody that is not expected to impact the cytochrome P450 enzymes. Also, zanidatamab is not known to target mechanisms related to proinflammatory cytokines or any mechanism related to proinflammatory cytokines that may impact the pharmacokinetics (PK) of concomitant medicines.

Additional comments

Nil

References

Ziihera SPC (accessed 8th May 2026) - https://www.medicines.org.uk/emc/product/101948/smpc

THIS PROTOCOL HAS BEEN DIRECTED BY DR MITCHELL, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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