HCF (Trastuzumab, Cisplatin and 5FU)

Indication

Locally advanced or metastatic adenocarcinoma of the stomach or gastro-oesophageal junction Tumours must be Her2 positive either 3+ on IHC or 2+ on IHC and positive on FISH (or similar) where there are indications to substitute capectiabine for 5FU.

Regimen details

Drug	Fluid	Time
Trastuzumab 8mg/kg cycle 1 only; 6mg/kg on subsequent cycles	250ml 0.9% sodium chloride	see below
	1 litre 0.9% sodium chloride + 20mmol potassium chloride + 10mmol magnesium sulphate	2 hours
Cisplatin 80mg/m2	1 litre 0.9% sodium chloride	2 hour
	1 litre 0.9% sodium chloride + 20mmol potassium chloride + 10mmol magnesium sulphate	2 hours
5-Fluorouracil 1000mg/m2 /day	0.9% sodium chloride	Continuous intravenous infusion over 96 hours

Trastuzumab should be administered over 90 minutes in cycle 1 then over 30 minutes for subsequent cycles. Patients should be observed closely for infusion related side effects or anaphylaxis during cycle 1.

Cycle frequency

21 days

Number of cycles

6 cycles in locally advanced or metastatic disease followed by maintenance IV Trastuzumab until progression

Pre-medication

Paracetamol 1g 30-60 minutes before treatment, and regularly for 24 hours after treatment

Emetogenicity

Highly emetogenic

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
Calculated creatinine clearance (Cockcroft and Gault)	14 days
LFT (including AST)	14 days

Assessment of LVEF within the normal range on ECHO or MUGA - measured at least 4 monthly

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle). Patients require DPD testing prior to administration. Dose adjustments should be made in accordance with local DPD policy

Investigations –pre subsequent cycles

FBC, U&Es, creatinine clearance (calculated), LFTs The liver function test may be retrospectively looked at (i.e. after the chemotherapy treatment) unless they are known to be abnormal then they need to be repeated the day before so that the results are available pre-chemotherapy

If serum creatinine raised >20% repeat calculated creatinine clearance before next cycle

MUGA scan or ECHO measured at least 4 monthly

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	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L (PLT 75-100 may go ahead at discretion of consultant)
Creatinine clearance	≥ 50 mL/min
Bilirubin	≤ 1.5 x ULN
AST, ALT	< 2.5 x ULN
Alk Phos	<2.5 x ULN

Dose modifications

Haematological Toxicity

Neutrophils (x109/l)	**Platelets (x109/l)**	**Action**
>1.0	> 100	Full Dose
<1.0	<100	Delay until recovery Restart 5FU and cisplatin at 75% dose
<0.5 and febrile requiring hospitalisation		Delay until recovery restart 5Fu and cisplatin at 50% dose

Renal Toxicity

	GFR (mL/min)	**Action**
Trastuzumab		No dose reduction necessary
Cisplatin	<50	Defer, consider Carboplatin AUC5
5-fluorouracil	30-50	Dose reduce by 25%
	<30	Omit

Adverse effects –

For full details consult product literature/ reference texts

Infusion related:

Mild – Chills and rigor, tumour site pain, nausea and vomiting, asthenia, headache, cardiotoxicity. Severe – Dyspnoea, hypotension, urticaria/angioedema, anaphylaxis Alopecia, Nephrotoxicity,

Tiredness, diarrhoea and abdominal pain, nausea and vomiting, sore mouth, poor appetite, myelosuppression and thrombocytopenia, hand foot syndrome, cardiotoxicity (including coronary artery spasm, angina and tachycardia), ocular toxicity (excessive lacrimation, visual change, photophobia), peripheral neuropathy, infusion reactions, pulmonary fibrosis, veno- occlusive disease, high tone and hearing loss, ovarian failure/infertility

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism- avoid use in patients with known DPD deficiency

Additional comments

Cautions

Caution if history of ischaemic heart disease Raised bilirubin or AST

Contra-indication

Patients experiencing dyspnoea at rest due to either co-morbidities or complications of advanced malignant disease should not receive trastuzumab.

References

ToGA trial 2010

THIS PROTOCOL HAS BEEN DIRECTED BY DR CATHERINE THOMPSON, DESIGNATED LEAD CLINICIAN FOR UPPER GI

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: 24/11/20
Review: 20/11/2023
VERSION: 1.