

# HCarboF (Trastuzumab, Carboplatin 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 cisplatin for carboplatin and capecitabine 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
Carboplatin AUC 5	500mL glucose 5%	1 hour
5-Fluorouracil 1000mg/m <sup>2</sup> /day	0.9% sodium chloride	Continuous 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.

5-Fluorouracil pump 800 mg/m<sup>2</sup>/day intravenous infusion every 3 weeks via pump device

## Cycle frequency

21 days

## Number of cycles

6 cycles in locally advanced or metastatic disease followed by maintenance trastuzumab until progression.

## Pre-medication

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

## Emetogenicity

Moderately 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

Calvert formula:  $(CrCl \text{ (ml/min)} + 25) \times AUC$

Cockcroft and Gault (for calculating creatinine clearance)

Female  $(140 - \text{age( yrs)}) \times \text{wt(kg)} \times 1.04$

Serum creatinine (micromol/l)

Male  $(140 - \text{age( yrs)}) \times \text{wt(kg)} \times 1.23$

Serum creatinine (micromol/l)

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	$\geq 1.0 \times 10^9/L$
Platelet count	$\geq 100 \times 10^9/L$ ( if PLT 75-100 can go ahead at discretion of consultant)
Creatinine clearance	$\geq 50 \text{ mL/min}$
Bilirubin	$\leq 1.5 \times \text{ULN}$
AST, ALT	$< 2.5 \times \text{ULN}$
Alk Phos	$< 2.5 \times \text{ULN}$

#### Dose modifications

##### Haematological Toxicity

Neutrophils (x10 <sup>9</sup> /l)	Platelets (x10 <sup>9</sup> /l)	Action
>1.0	> 100	Full Dose
<1.0	<100	Delay until recovery Restart 5FU and carboplatin at 75% dose
<0.5 and febrile requiring hospitalisation		Delay until recovery restart 5Fu and carboplatin at 50% dose

##### Renal Toxicity

	GFR (mL/min)	Action
Trastuzumab		No dose reduction necessary
Carboplatin	<20	Omit
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

The Calvert formula is not considered reliable if the creatinine clearance is <40 ml/min. However, prescribing according to surface area leads to excessive doses. Therefore, even in those patients with renal impairment the Calvert formula will be used and doses modified subsequently up or down depending on blood counts

### Contra-indication

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

## References

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**THIS PROTOCOL HAS BEEN DIRECTED BY DR CATHERINE THOMPSON, on behalf of DR CATHERINE MITCHELL DESIGNATED LEAD CLINICIAN FOR UPPER GI**

**RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE**

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