North West Coast
Strategic Clinical Networks

Chemotherapy protocol

Drug regimen
ECF

Indications for use
As for ECX regimen (see protocol), for patients intolerant of capecitabine

Regimen

Drug	Route	Fluid	Time
Epirubicin 50mg/m^2	IV		IV bolus
	IV	1 litre 0.9% sodium chloride + 20mmol potassium chloride + 10mmol magnesium sulphate	2 hours
Cisplatin 60mg/m^2	IV	500ml 0.9% sodium chloride	1 hour
	IV	1 litre 0.9% sodium chloride + 20mmol potassium chloride + 10mmol magnesium sulphate	2 hours
5-fluorouracil 200mg/m^2/day	IV		IV infusor over 21 days

Day 8 and Day 15, 5-Fluourouracil pump changes
Regimen to be repeated 3 weekly

Investigation prior to initiating treatment
FBC
Day 8 and Day 15, 5-Fluourouracil pump changes, obtain FBC but continue with pump unless patient is clinically unwell. Consider prophylactic antibiotics if neutrophils are low.
Biochemical profile
Calculated creatinine clearance (Cl_{Cr})
MUGA scan for pre-op patients over 55 years old
MUGA scan for palliative patients with pre-existing cardiac disease only

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.

Cautions
Caution if history of ischaemic heart disease.
Raised bilirubin or AST

Investigations and consultations prior to each cycle
FBC – weekly
U&Es, calculated creatinine clearance, LFTs - 3 weekly prior to cisplatin
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

Acceptable limits for treatment to proceed (if outside these delay one week or contact consultant)
Neutrophils $\geq$1.0 and platelets $\geq$75

Creatinine Clearance ≥50ml/min

Bilirubin <1.5 x ULN, ALT, AST < 2.5 ULN, Alk Phos < 2.5 ULN

Side Effects

Alopeica, 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

Dose Modification Criteria

Haematological Toxicity

Neutrophils ($x10^9$/l)	**Platelets ($x10^9$/l)**	**Action**
>1.0	> 75	Full Dose
0.5 - 0.9	50-74	Delay until recovery Restart 5-Flurouracil and cisplatin at full dose Reduce Epirubicin by 25%
< 0.5	25-49	Delay until recovery Restart 5-Flurouracil and cisplatin at full dose Reduce Epirubicin by 50%
	<25	Delay until recovery Restart 5-Flurouracil and cisplatin at full dose Omit Epirubicin from subsequent cycles

Renal

Result	**GFR (ml/min)**	**Action**
Epirubicin		No dose reduction necessary
Cisplatin	<50	Defer and consider carboplatin AUC 5
5-fluorouracil	30-50	Dose reduce by 25%
	<30	Omit

Palmar-plantar erythema (PPE):

Palmar Plantar Erythrodysaesthesia	**Grade**	**Action**
	1	No dose reduction necessary
	2	Delay 5-Flurouracil until resolved to grade 0-1 then restart at 15% dose reduction
	3	Delay 5-Flurouracil until resolved to grade 0-1 then restart at 30% dose reduction

Liver function
If bilirubin increases to > 1.5 ULN, epirubicin should be omitted until bilirubin returns to acceptable levels

Non-haematological toxicity: stomatitis, diarrhoea, nausea & vomiting

(See separate section for palmar-plantar syndrome)

For grade 2-3 toxicity, stop fluorouracil and administer appropriate symptomatic management. If toxicity is adequately controlled with symptomatic measures alone within 2 days, then fluorouracil may be restarted at 100% full dose. If toxicity persists, the following dose reductions should be made:

	Grade 2	**Grade 3**	**Grade 4**
1st appearance	Interrupt treatment until resolved to grade 0-1 then continue at same dose. .	Interrupt treatment until resolved to grade 0-1 then continue at 75% of original dose with prophylaxis where possible	Discontinue treatment unless consultant considers it to be in the best interest of the patient to continue at 50% of original dose once toxicity has resolved to grade 0-1.
2nd appearance of same toxicity	Interrupt treatment until resolved to grade 0-1 then continue at 75% of original dose	Interrupt treatment until resolved to grade 0-1 then continue at 50% of original dose	
3rd appearance of same toxicity	Interrupt treatment until resolved to grade 0-1 then continue at 50% of original dose	Discontinue treatment	
4th appearance of same toxicity	Discontinue treatment		

Specific Information on Administration
Epirubicin is a vesicant and must be administered first.
Patients should be informed of the need to interrupt treatment immediately if they develop moderate or severe side effects particularly diarrhoea (not controlled by loperamide), palmar plantar erythrodyaesthesia, chest pain or infection.

References

D. Cunningham el al NCRI Upper GI Study Group Randomised multicentre phase III study comparing capecitabine with 5FU and oxaliplatin with cisplatin in patients with advanced oesophagogastric (OG) cancer: The REAL 2 trial N Engl J Med 2010; 362:858-859

THIS PROTOCOL HAS BEEN DIRECTED BY DR MITCHELL DESIGNATED LEAD CLINICIAN FOR UPPER GI CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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