NHS
North West Coast
Strategic Clinical Networks

Chemotherapy protocol

DRUG REGIMEN
Gemcitabine / capecitabine 28 day cycle

Indication for use
Adjuvant treatment for pancreatic carcinoma post-surgery
Locally advanced or metastatic carcinoma of the pancreas

Regimen

Day	Drug	Route	Fluid	Time
1	Gemcitabine 1000mg/m^2	IV	250ml 0.9% sodium chloride	30 minutes
8	Gemcitabine 1000mg/m^2	IV	250ml 0.9% sodium chloride	30 minutes
15	Gemcitabine 1000mg/m^2	IV	250ml 0.9% sodium chloride	30 minutes

Days 1-21: capecitabine 830mg/m^2 bd

Given every 28 days for 6 cycles

Investigation prior to initiating treatment
FBC
Biochemistry including LFTs
Ca 19-9

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
Raised bilirubin or AST

Investigations and consultations prior to each cycle
FBC (prior to each cycle and on days 8 & 15 pre-gemcitabine)
U&Es
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

Consultation day 1 of each cycle

Acceptable levels for treatment to proceed

Neutrophils ≥ 1.5 and platelets ≥ 100

If neutrophils <1.5 contact consultant

For adjuvant patients:
If consultant not contactable and ANC > 1.0 continue with full dose.
If ANC <1.0, defer by 1 week.

For metastatic patients:

If consultant not contactable and ANC < 1.5, defer by 1 week.

Side Effects
Myelosuppression – all cell lines

Occasionally: Rash and mild SOB, 'flu like' symptoms
Gastro-intestinal toxicity-nausea, vomiting, diarrhoea and constipation
Skin toxicity-hand foot syndrome, skin rash
CVS-LL oedema, chest pain, angina
Haematological- low Hb and neutropenia
General-fatigue, pyrexia, anorexia, conjunctivitis

Rarely: severe dyspnoea (ARDS), haemolytic ureaemic syndrome; **discontinue if these occur**

Dose Modification Criteria in the Adjuvant Setting

Haematological Toxicity – Dose Adjustment Absolute neutrophil count (x10^9/l)	**Gemcitabine dose modification**
> 1.0	100% of full dose
0.5 – 1.0	75% of full dose
<0.5	Omit for one week
Platelet count (x10^9/l)	**Gemcitabine dose modification**
> 100	100% of full dose
50 – 100	75% of full dose
<50	Omit for one week

Clinical Scenario	**Gemcitabine dose for next treatment**	**Capecitabine dose for next treatment**
Dose reduction for one week	Dose according to neutrophil and/or platelet count on that day	Continue 100%
Dose reduction for two consecutive weeks	75% of full dose with no re-escalation	Continue 100%
Initial dose omission for one week	75% of full dose with no re-escalation	Continue 100%
Recurrent dose omission or delay ≥ two weeks	75% of full dose with no re-escalation	75% of full dose with no re-escalation

Dose Modification for Capecitabine Grading according to NCI-CTCAE v3.0	**Occurrence**	**Action**	**Dose adjustment for next cycle (% of starting dose)**

Grade 1		Supportive measures	100%
Grade 2	First appearance	Interrupt until resolved to grade 0-1	100%
	Second appearance	Interrupt until resolved to grade 0-1	75%
	Third appearance	Discontinue	N/A
Grade 3	First appearance	Interrupt until resolved to grade 0-1	75%
	Second appearance	Interrupt until resolved to grade 0-1	50%
	Third appearance	Discontinue	
Grade 4	First appearance	Discontinue permanently	Discontinue

Renal Impairment
For patients with mild renal impairment (creatinine clearance 51-80ml/minute), no dose adjustment is necessary. For patients developing moderate renal impairment (creatinine clearance between 30-50ml/min) during treatment, a 25% dose reduction should be made to the dose of capecitabine. Patients who develop severe renal impairment (creatinine clearance <30ml/min) should be withdrawn from trial treatment.

Hepatic impairment
In the absence of safety and efficacy data in patients with hepatic impairment, Capecitabine use should be carefully monitored in patients with mild to moderate liver dysfunction. Administration of Capecitabine should be interrupted if treatment-related elevations in bilirubin of >3.0 x ULN or treatment-related elevations in hepatic aminotransferases (ALT, AST) of > 2.5 x ULN occur. Treatment with Capecitabine may be resumed when bilirubin decreases to 3.0 x ULN or hepatic aminotransferases decrease to 2.5 x ULN.

Specific Information on Administration
Gemcitabine:
30 minute infusion in 0.9% Sodium Chloride 250mls (longer infusion times lead to increased toxicity)

Capecitabine:
Tablets should be swallowed with water within 30 minutes after a meal

THIS PROTOCOL HAS BEEN DIRECTED BY DR MITCHELL DESIGNATED SUB LEAD FOR PANCREATIC CANCER AND APPROVED BY DR YOUNG DESIGNATED LEAD CLINICIAN FOR UPPER GI CANCER RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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References
ESPAC- 4 trial protocol

Cunningham D, Chau I, Stocken DD, et al. *(2009) Phase III randomized comparison of gemcitabine versus gemcitabine plus capecitabine in patients with advanced pancreatic cancer. J Clin Oncol 27:5513–5518*

Metastatic Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline 2006