Systemic Anti Cancer Therapy Protocol

Gemcitabine & Capecitabine

Repeated every 28 days for 6 cycles (adjuvant) or until disease progression

PROTOCOL REF: MPHAGEMCAP
(Version No: 2.1)

Approved for use in

Adjuvant following resected adenocarcinoma of pancreas

First line treatment of locally advanced or metastatic adenocarcinoma of pancreas

Dosage

Drug	Dose	Route	Frequency
Gemcitabine	1000mg/m^2	IV	Days 1, 8 and 15 of 28 day cycle
Capecitabine	825mg/m^2 BD	PO	Days 1 to 21

Supportive Treatments:

Domperidone 10mg TDS PRN

Loperamide 4mg at onset then 2mg after each loose stool (max.16mg in 24hrs)

Thromboprophylaxis:

In line with recent NICE recommendations, patients with pancreatic cancer receiving chemotherapy should receive thromboprophylaxis with a LMWH unless contra-indicated. Contra-indications include high bleeding-risk. The decision regarding thromboprophylaxis as part of chemotherapy has to be clearly documented by the consultant.

- Dalteparin 5000 IU by subcutaneous injection once daily

Extravasation risk

Gemcitabine

NEUTRAL – no action necessary

Refer to Clatterbridge Policy 'Prevention and Management of Extravasation Injuries' for further guidance.

Administration

Day	Drug	Dose	Route	Diluent and rate
1	**Dexamethasone** 30mins before chemotherapy	**8mg**	**PO**	
	Gemcitabine	**1000mg/m^2**	**IV**	**250ml Sodium Chloride 0.9% over 30 minutes**
8	**Dexamethasone** 30mins before chemotherapy	**8mg**	**PO**	
	Gemcitabine	**1000mg/m^2**	**IV**	**250ml Sodium Chloride 0.9% over 30 minutes**
15	**Dexamethasone** 30mins before chemotherapy	**8mg**	**PO**	
	Gemcitabine	**1000mg/m^2**	**IV**	**250ml Sodium Chloride 0.9% over 30 minutes**
1-21	**Capecitabine**	**825mg/m^2**	**PO**	**Twice Daily (morning and evening) for 21 days**
22	**NO TREATMENT**			

Capecitabine is available in 500mg and 150mg tablets.

Capecitabine should be taken with water within 30 minutes after food. For patients unable to swallow tablets, capecitabine can be dissolved in warm water (stirring until tablets completely dispersed).

Main Toxicities

Gemcitabine
Nausea, vomiting, fatigue, diarrhoea, constipation, alopecia, peripheral oedema, rash, influenza-like symptoms, dizziness during infusion, peripheral neuropathy, stomatitis. Neutropenia, thrombocytopenia, anaemia, elevated liver function tests, haematuria and proteinuria
Capecitabine
Diarrhoea, nausea, vomiting, stomatitis, abdominal pain, dyspepsia, alopecia, rash, dry skin, pruritus, hyperpigmentation, palmer-plantar erythema, insomnia, depression, headache, dizziness. Neutropenia, thrombocytopenia, anaemia, elevated liver function tests. Cardiotoxicity (including myocardial infarction, angina and arrhythmias).

Investigations and Treatment Plan

		C1 D1	Pre	C1 D15	C2 D1	C2 D8	C2 D15	Ongoing
Clinical Assessment	X	X			X			For palliative, alternate cycles.
SACT Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	Repeat if clinically indicated
Magnesium	X	X			X			Every cycle
Random blood glucose	X	X			X			Every cycle
CA19.9	X	X			X			Every cycle
Dihydropyrimidine dehydrogenase (DPD) deficiency test	X							This test is normally only required if a patient has not had capecitabine, or fluorouracil in the past. However a consultant may still request this test if capecitabine or fluorouracil was not tolerated previously. The result must be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary. Treatment with capecitabine and fluorouracil is contraindicated in patients with known complete DPD deficiency.
CT scan	X							Every 12 weeks
Informed Consent	X							
Blood pressure*	X							Repeat if clinically indicated
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle
Height recorded	X							

Dose Modifications and Toxicity Management

Haematological Toxicity

Day of Treatment	FBC			Treatment Delay
	ANC	AND/ OR	PLT	
Day 1	≥ 1.0		≥ 75	Proceed with treatment
	< 1.0		< 75	Delay treatment until counts recovered
Day 8	≥ 1.0		≥ 75	Proceed with treatment
	0.5 - 0.9		50 - 74	Discuss with clinician. Dose reduce by 25%
	< 0.5		< 50	OMIT
Day 15	≥ 1.0		≥ 75	Proceed with treatment
	0.5 - 0.9		50 - 74	Discuss with clinician. Dose reduce by 25%
	< 0.5		< 50	OMIT

If day 1 is deferred or days 8 or 15 reduced/omitted on more than two occasions, discuss with clinician and consider an overall dose reduction by 20-25%.

Non-haematological Toxicity

Toxicity (CTC Grade)	Treatment Delay	Appearance	Dose Reduction
Grade 1	No delay	-	No reduction
Grade 2	Delay until Grade 1 or better	1st	No reduction
		2nd	Resume at 75%
		3rd	Resume at 50%
Grade 3		1st	Resume at 75%
		2nd	Resume at 50%
		3rd	Discontinue
Grade 4	-	1st	Discontinue

Hepatic impairment

Gemcitabine
No safety data in patients with hepatic impairment. If bilirubin > 27µmol/L, consider reducing dose to 800mg/m^2.
Capecitabine
Insufficient safety and efficiency data are available in patients with hepatic impairment.

Renal impairment

Gemcitabine
No safety data in patients with CrCl < 30ml/min. Consider dose reduction (clinical decision).
Capecitabine
Contraindicated in patients with severe renal impairment (CrCl < 30 ml/min). Incidence of grade 3 or 4 adverse reactions is increased in patients with moderate renal impairment (CrCl 30-50 ml/min however no dose reduction is required at the start of treatment (due to the lower dose being used in this regimen).

Drug Interactions

Gemcitabine
Warfarin/coumarin anti-coagulants – can increase anticoagulant effect or cause fluctuations. Avoid if possible or consider switching patient to a LMWH during treatment. If patient continues to take an oral anticoagulant, INR must be checked at least once a week and dose adjusted accordingly. Gemcitabine is a radio-sensitiser.
Capecitabine
Warfarin/coumarin anti-coagulants – can increase anticoagulant effect. Avoid if possible or consider switching patient to a LMWH during treatment. **Phenytoin** - Capecitabine may increase the serum concentration of Phenytoin. A reduction in phenytoin dose may be necessary. Monitor phenytoin concentrations and response to therapy closely (both effectiveness and signs/symptoms of toxicity). **Folinates** – can enhance the toxicity of capecitabine. Avoid concomitant use of folinic and folic acid.

References:

1. Gemcitabine 100mg/ml Concentrate for solution for infusion. Summary of Product Characteristics. Accord Healthcare Ltd, Middlesex, 06/06/2012. Available from https://www.medicines.org.uk/emc last updated 01/11/2012.
2. Xeloda 150mg and 500mg film-coated tablets. Summary of Product Characteristics. Roche Registration Ltd, Welwyn Garden City, 02/02/2006. Available from https://www.medicines.org.uk/emc last updated 22/01/2015.
3. Dosage Adjustment for Cytotoxics in Renal and Hepatic Impairment. University College London Hospital NHS Foundation Trust January 2009.
4. Cancer Chemotherapy: Guidelines for the administration of chemotherapy and the nursing care of cancer patients (6th Edition)
5. NICE guideline NG89. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (August 2019)