Systemic Anti Cancer Treatment Protocol

Gemcitabine Oxaliplatin (GEMOX)

PROTOCOL REF: MPHAGEOXGC
(Version No: 1.0)

Approved for use in:

Palliative treatment for relapsed Germ Cell Tumours (metastatic seminoma, non-seminoma or combined tumours)

Dosage:

Drug	Dosage	Route	Frequency
Gemcitabine	1000mg/m^2	IV	Day 1 and 8 of a 21 day cycle
Oxaliplatin	130mg/m^2	IV	Day 1 of a 21 day cycle

Usually up to 6-8 cycles but can be given until progression or unacceptable toxicity (Reassess after 6 cycles and continue at consultant's discretion).

Supportive treatments:

Antiemetic Risk – Moderate – follow antiemetic policy

Domperidone 10mg oral tablets, up to 3 times a day or as required

Extravasation risk:

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Gemcitabine – neutral

Oxaliplatin – irritant

Administration:

Day	Drug	Dosage	Route	Diluent and Rate
1	**Dexamethasone** 30 mins before chemotherapy	8mg	PO	
	Ondansetron 30 mins before chemotherapy	16mg	PO	
	Line flush with 0.9% Sodium Chloride			
	Gemcitabine	1000mg/m^2	IV	Sodium Chloride 0.9% 250mL over 30 minutes
	Line flush with 5% Glucose			
	Oxaliplatin	130mg/m^2	IV	Glucose 5% 500mL over 120 minutes (in 250mL for doses less than 100mg)
8	**Dexamethasone** 30 mins before chemotherapy	8mg	PO	
	Gemcitabine	1000mg/m^2	IV	Sodium Chloride 0.9% 250mL over 30 minutes

Notes:

Be aware of possible platinum hypersensitivity related reactions with oxaliplatin and administer pre-meds as prescribed

Caution in patients with pre-existing neurotoxicity

Caution in patients with pre-existing heart disease, angina pectoris, arrhythmias

Correct any magnesium deficiency before giving oxaliplatin

Main Toxicities:

Oxaliplatin

Infusion reactions, neuro toxicity, myelosuppression, mucocitis, diarrhoea, nausea and vomiting

Gemcitabine

Myelosuppression, anaemia, anorexia, breathlessness, oedema, rash, itchy skin, hair loss, fatigue.

Investigations and treatment plan

	Pre	Cycle 1	All cycles day 8	Cycle 2	Cycle 3	Cycle 4	Ongoing
Informed Consent	X						
Clinical Assessment	X			X		X	Alternate cycles
SACT assessment (including PS and toxicities)	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	Every cycle
U&E, LFT and magnesium	X	X	X	X	X	X	Every cycle
CrCl	X	X		X	X	X	Every cycle
CT scan	X						As clinically indicated
ECG							If clinically indicated
Blood pressure	X						Repeat if clinically indicated
Respiratory rate	X						Repeat if clinically indicated
Weight recorded	X	X	X	X	X	X	Every cycle
Height recorded	X						
AFP, HCG, LDH (LDH at Pre/Cycle 1 only)	X	X		X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Day 1

Proceed on day 1 if all apply:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 75 x 10^9/L

Delay 1 week on day 1 if any apply:-

ANC ≤ 0.9 x 10^9/L	Platelets ≤ 74 x 10^9/L

Day 8

Proceed on day 8 if

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 75 x 10^9/L

Discuss with clinician if *

ANC 0.5-0.9 x 10^9/L	Platelets 50-74 x 10^9/L

Omit gemcitabine if *

ANC < 0.5 x 10^9/L	Platelets < 50 x 10^9/L

* re-start next cycle with 75% dose- at discretion of clinician

Non-haematological toxicity

<table>
<tr><td>Renal</td><td>Calculate CrCl using Cockroft and Gault before each cycle. If renal function falls by >30% than expected value consider EDTA clearance
<table>
<tr><th>Creatinine Clearance (mL/min)</th><th>Oxaliplatin Dose</th><th>Gemcitabine Dose</th></tr>
<tr><td>>50</td><td>100%</td><td>100%</td></tr>
<tr><td>30 to 50</td><td>Max 85mg/m^2</td><td>100%</td></tr>
<tr><td><30</td><td>Consultant decision, consider 50%</td><td>Consultant decision, no need for dose adjustment is expected</td></tr>
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Hepatic	**Liver function**	**Oxaliplatin dose**	**Gemcitabine Dose**
	Bilirubin < 27 µmol/L	100%	100%
	Bilirubin ≥ 27 µmol/L	100%	Start at 80%

Oxaliplatin	
Neurotoxicity – see notes below for specific cases	<table><tr><td>Neurotoxicity</td><td>Oxaliplatin dose</td></tr><tr><td>Grade 1 any duration or grade 2 < 7days but resolving before next cycle</td><td>100%</td></tr><tr><td>Grade 2 persisting until next cycle – at clinician's discretion</td><td>75%</td></tr><tr><td>Grade 3 <7 days but resolved before the next cycle- at clinician's discretion</td><td>75%</td></tr><tr><td>Grade 3 persisting to next cycle or any grade 4</td><td>Consider stopping oxaliplatin</td></tr></table>
Acute cold related dysaesthesia (CRD)	Transient paraesthesia of hands and feet as well as laryngopharyngeal dysaesthesia (unpleasant sensations in throat) is common. Onset is during or within hours of infusion and it resolves in minutes or days. Symptoms are exacerbated by cold – advise patients on suitable precautions e.g. avoid cold drinks. Should not require dose reduction, but if troublesome then infusion duration can be increased to 6 hours (see note below). Consider applying heat pad to painful areas.
Laryngopharyngeal dysaesthesia	Characterized by loss of sensation of breathing without any objective evidence of distress (hypoxia, laryngospasm or bronchospasm). May be exacerbated by cold air. If this occurs during the infusion, stop the infusion immediately and observe the patient. Resolution is relatively rapid (within minutes to a few hours). Check oxygen saturation; if normal an anxiolytic agent may be given. The infusion can be restarted at a slower rate at the clinicians' discretion.
Cumulative dose related sensory neuropathy	Usually occurs after a cumulative dose of 800mg/m^2. It can occur after treatment is completed, is usually reversible taking about 3-5 months to recover
Allergic reactions during infusion	Stop the infusion and call for help. Follow trust anaphylaxis policy. Treat with IV corticosteroid and antihistamine. Discuss discontinuing or re-challenge with the consultant.

Whilst the recommended increase in duration of infusion is to 6 hours – where the oncologist and the treating team agree, this can be reduced to 4 hours dependent on the severity of the reaction and the tolerability of the infusion over this time.

<table>
<tr><th colspan="2">Gemcitabine</th></tr>
<tr><td>Diarrhoea & Stomatitis</td><td>
<table>
<tr><th>Toxicity (CTC Grade)</th><th>Treatment Delay</th><th>Dose Reduction</th></tr>
<tr><td>Grade 1</td><td>No delay</td><td>No reduction</td></tr>
<tr><td>Grade 2</td><td rowspan="3">Delay until Grade 1 or better</td><td>No reduction</td></tr>
<tr><td>Grade 3</td><td>Resume at 75%</td></tr>
<tr><td>Grade 4</td><td>Resume at 50%</td></tr>
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</td></tr>
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References:

Southwest Strategic Clinical Network,Oxaliplaatin and Gemcitabine – germ cell. 2016. Avaliable at http://www.swscn.org.uk/wp/wp-content/uploads/2014/12/Oxaliplatin-and-Gemcitabine.pdf

Kollmansberger, C. et al. Combination chemotherapy with gemcitabine plus oxaliplatin in patients with intensively pretreated or refractory germ cell cancer: A study of the German testicular cancer study group (2004). J Clin Oncol 22: 108-14

Pectasides, D. et al. Gemcitabine and oxaliplatin (GEMOX) in patients with cisplatin-refractory germ cell tumours: a phase II study (2004). Ann Oncol; 15:493-97 Dosage

Supplement to: Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; **20:** e201–08.

Accord, Oxaliplatin 5mg/ml concentrate for Solution for Infusion SmPC, 2019 (cited March 2021) Available from: https://www.medicines.org.uk/emc/product/6088/smpc