

## GEMCITABINE, CISPLATIN, DEXAMETHASONE (Based on Baetz et al, Ann Oncol 2003)

**INDICATION:** Relapsed or refractory Hodgkin's and non-Hodgkin's lymphoma

### Prior to a course:

- Calculate creatinine clearance. If < 60ml/min *see dose modification and discuss with consultant*
- Patient should have adequate bone marrow reserve before commencing treatment, i.e neuts >1.0, platelets >100, unless due to marrow infiltration, splenomegaly.- *if not discuss with consultant*
- Use gemcitabine with caution if LFTs abnormal – *discuss with consultant & see dose modification*
- **If PBSC harvest planned** inform blood transfusion laboratory that further blood and platelet transfusions must be irradiated beginning from 7 days prior to PBSC harvest until completion. Assess venous access or arrange for femoral venous line following 3<sup>rd</sup> cycle with a view to apheresis
- Written consent for course

### Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Check FBC on day 1 & 8 – neutrophils must be > 1.0 and platelets >50 prior to each cycle. *See dose modifications*. Note there are no dose modifications for day 8 FBC.
- Check U&Es, creat, Ca, Mg, LFTs and creatinine clearance – *see dose modifications*
- Ensure patient is well hydrated and start monitoring urine output

<b>Day 1</b>	Gemcitabine	1000mg/m <sup>2</sup>	IV	in 250ml N saline over 30mins
	Cisplatin	75mg/m <sup>2</sup>	IV	In 1.0L N saline over ~ 2 hrs (1mg/min)
	<u>Cisplatin and hydration</u>			
	T – 2.5 hr	1.0L N saline (+20mmol KCL+10mmol MgSO <sub>4</sub> ) over 2hr		
	T – 30mins	10% Mannitol 125ml IV over 30mins - <i>check urine output &gt;100ml/hr</i>		
	T = 0 - 2hrs	Cisplatin 75mg/m <sup>2</sup> in 1.0L N saline by IV infusion at 1mg/min (approx. 2hrs)		
	T = +2hrs	1.0L N saline (+20mmol KCL+10mmol MgSO <sub>4</sub> ) over 2 hrs		
	<i>Maintain urine output of at least 100ml/hr – repeat 10% mannitol if necessary</i>			
<b>Days 1-4</b>	Dexamethasone	40mg od PO	or	IV in 100ml N saline over 15mins
<b>Day 8</b>	Gemcitabine	1000mg/m <sup>2</sup>	IV	in 250ml N saline over 30mins
<b>Day 9 - 16</b>	GCSF	5µg/kg od	SC	

**Repeat cycle every 21 days for 2 - 6 cycles**

### Prophylaxis for acute emesis

Give dexamethasone first + 5HT antagonist

### Prophylaxis for delayed emesis

5HT antagonist + metoclopramide

### Other medications

Allopurinol 300mg od for 5 days with cycle 1

Anti-infective prophylaxis according to local policy

**Dose modification for haematological toxicity (day 1 only)**

- There are no dose reductions in subsequent cycles but on day 1 neutrophils must be  $> 1.0$  and platelets  $>50$  prior to each cycle.
- If treatment is delayed by  $\geq 2$  weeks or patient has neutropenic sepsis despite primary GCSF prophylaxis, consider whether further treatment is appropriate or reduce gemcitabine to 50-75% dose – *discuss with consultant*.

**Dose modification for neurological toxicity**

- In case of grade 1 toxicity to cisplatin - peripheral neuropathy (paraesthesia not interfering with function) or constipation, visual changes or tinnitus. Reduce dose to  $50\text{mg}/\text{m}^2$  per cycle
- If the neurological toxicity increases despite reduced dosage. Discontinue cisplatin permanently

**Dose modification for renal toxicity**

- If day 1 creat  $>300\mu\text{mol}/\text{l}$  delay for 1-2 weeks
- If day 1 creat  $< 300\mu\text{mol}/\text{l}$  adjust cisplatin & gemcitabine as follows:
 

Cr.Cl $>60\text{ml}/\text{min}$	100% dose cisplatin & gemcitabine
Cr.Cl $45\text{-}60\text{ml}/\text{min}$	$37.5\text{mg}/\text{m}^2$ cisplatin days 1 & 8, 100% gemcitabine
Cr.Cl $<45\text{ml}/\text{min}$	Delay until CrCl recovers to $>45\text{ml}/\text{min}$ or consider using carboplatin – <i>discuss with consultant</i>
- If day 1 creatinine  $>300\mu\text{mol}/\text{l}$  omit day 8 gemcitabine

**Dose modification for abnormal liver function**

- If bilirubin  $>27\mu\text{mol}/\text{L}$  there is an increased risk of hepatic toxicity due to gemcitabine. Consider starting at a reduce dose of gemcitabine  $800\text{mg}/\text{m}^2$  and escalating according to tolerance.

**Gem-Cis-Dex Toxicities**

Neutropenic sepsis	Nausea& vomiting (moderate - severe)
Thrombocytopenia	Amenorrhoea & infertility (offer semen cryopreservation)
Mucositis	Nephrotoxicity
Alopecia	Peripheral neuropathy
Ototoxicity	Haemolytic-uraemic syndrome (gemcitabine)
Somnolence & fatigue (gemcitabine)	Liver dysfunction (gemcitabine)
Rash & pruritus	Dyspnoea – pneumonitis secondary to gemcitabine
Proteinuria & haematuria	

**Written by** Dr MP Macheta, Consultant Haematologist

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