GEMCITABINE & DOCETAXEL

Second-line use in metastatic soft tissue sarcomas

Drug / Dosage:	Gemcitabine	900mg/m^2	IV	Day 1 and Day 8
	Docetaxel	100mg/m^2	IV	Day 8 only (given after gemcitabine)
	Primary G-CSF prophylaxis		s/c	once daily for 7 days, starting on Day 9
	Patients with prior pelvic radiation:			
	Gemcitabine	675mg/m^2	IV	Day 1 and Day 8
	Docetaxel	75mg/m^2	IV	Day 8 only (given after gemcitabine)
	Primary G-CSF prophylaxis		s/c	once daily for 7 days, starting on Day 9

Administration: Gemcitabine in 250ml 0.9% sodium chloride over **90** minutes
Docetaxel in 250ml 0.9% sodium chloride over 1 hour

Frequency: 3 weekly cycle for 6 cycles

Main Toxicities: hypersensitivity reactions (docetaxel infusion-related);
myelosuppression; alopecia; fluid retention; stomatitis;
skin reactions & nail changes; peripheral neurotoxicity; diarrhoea; myalgia/arthralgia;
erythematous rash; flu-like syndrome;
peripheral oedema (mild –moderate & reversible); ovarian failure/infertility

Anti-emetics: Day 1 mildly emetogenic; Day 8 moderately emetogenic

Extravasation: non-vesicants

Regular Investigations:	FBC	Day 1
	LFTs	Day 1
	U&Es	Day 1

Comments: Docetaxel pre-medication (to prevent hypersensitivity reactions and fluid retention):
Dexamethasone 8 mg po bd for 3 days, commencing the morning of Day 7.

If the patient has not taken the oral pre-med for any reason, intravenous dexamethasone is not recommended and can only be substituted if prescribed by a Consultant.

Offer scalp cooling for Day 8 docetaxel

Dose Modifications

Haematological Toxicity:

Day 1:	Neutrophils < 1.0 x 10^9/l or Platelets < 100 x 10^9/l	Delay for 1 week. Repeat FBC. If recovered to above these limits, continue with full dose treatment. If no recovery after 2 weeks, review treatment.

Reason for Update: G-CSF dosing reviewed	Approved by Consultant: Dr A Neal
Version: 3	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 2	Date: 11.5.15
Prepared by: S Taylor	Checked by: C Tucker

Day 8:

Neutrophils		Platelets	Doses
≥ 1.0 x 10^9/l	and	≥ 100 x 10^9/l	Give 100% doses
0.5 – 0.99 x 10^9/l	or	50 - 99 x 10^9/l with no evidence of bleeding	Give 75% doses of both gemcitabine and docetaxel.
< 0.5 x 10^9/l	or	< 50 x 10^9/l	Omit **(Do not defer)**

At any time: If patient has febrile neutropenia or platelets < 25 x 10^9/l for more than 5 days, give 25% dose reduction of docetaxel and gemcitabine for all further cycles. If this problem re-occurs at the lower dose, the treatment should be discontinued.

Renal Impairment: If CrCl < 30ml/min, consider gemcitabine dose reduction – clinical decision

Hepatic Impairment:

ALT/AST > 1.5 x ULN
and
ALP > 2.5 x ULN
→ Give Docetaxel 75mg/m^2

Bilirubin > 22 µmol/l
or
ALT/AST > 3.5 x ULN
with
ALP > 6 x ULN
→ Docetaxel should not be administered without consultant approval

If bilirubin > 27 µmol/L, consider initiating treatment with a reduced dose of gemcitabine.

Other toxicities: If Grade 3 or 4 neurotoxicity, delay treatment for 1 week. If neurotoxicity resolves to ≤ Grade 2, treatment may be restarted, with docetaxel dose reduced to 75% of previous dose for all remaining cycles. If symptoms return, stop docetaxel.

If Grade 3 or 4 cutaneous reactions, once patient recovered, reduce docetaxel dose to 75mg/m^2. If symptoms return, stop docetaxel.

Docetaxel-induced myalgia and arthralgia often co-exist, usually Grade 1 or Grade 2. Management consists of reassuring patients that it is self-limiting. Consider use of NSAIDs, although not always effective.

References:

Hensley, ML et al; JCO 2002; 15 (20): 2824 – 2831
Maki, RG et al; JCO 2007; 25 (19): 2755 – 2763
Hensley, ML et al; Gynecol Oncol 2008; 109 (3): 329 – 334
Hensley, ML et al; Gynecol Oncol 2008; 109 (3): 323 – 328
Leu, KM et al; JCO 2004; 22 (9) : 1706 - 1712