PROTOCOL

Systemic Anti Cancer Therapy Protocol

Gemcitabine and docetaxel Sarcoma

PROTOCOL REF: MPHAGEMDOC
(Version No. 1.3)

Approved for use in:

- Osteosarcoma- 3rd line
- Ewing's family sarcoma- 2nd and 3rd line
- Soft tissue sarcomas including: leiomyosarcoma, uterine leiomyosarcoma- 2nd line
- Bone sarcoma-2nd or 3rd line
- Desmoplastic small round cell tumour-2nd line

Dosage:

Drug	Dose	Route	Frequency
Gemcitabine*	**675 mg/m^2**	IV infusion	Day 1 and 8 of a 21 day cycle
Docetaxel**	**75 mg/m^2**	IV infusion	Day 8 of a 21 cycle

Give for 6 cycles and review – may be continued for 8 cycles subject to tolerance, efficacy and patient preference

In bone or osteoscarcoma dose escalations may be considered in patient who tolerate treatment well

*Gemcitabine 900mg/m^2

**Docetaxel 100mg/m^2

Administration:

Docetaxel

- Ensure pre-med dexamethasone has been prescribed and taken before docetaxel.
- If dexamethasone pre-meds have not been taken then dexamethasone IV 13.3mg may be administered prior to starting the docetaxel infusion.
- Dexamethasone anti-emetics not needed as part of pre-med regimen hypersensitivity reactions to docetaxel normally occur within the first few minutes of the initiation of the infusion. Facilities to treat anaphylaxis must be present when administering this regimen. If a patient experiences an infusion-related reaction, give future does with premedication cover of **IV chlorphenamine 10mg and IV hydrocortisone 100mg.**

Gemcitabine

Do not give concurrent radiotherapy with gemcitabine Note: Beware of possible pulmonary symptoms of cough and breathlessness –see toxicity management.

Poor lung function prior to treatment is a relative contraindication

Emetogenic risk:

Low emetogenic.

Supportive treatments:

- Dexamethasone tablets 8mg twice a day for three days starting 24 hours before docetaxel
- Metoclopramide 10mg tablets up to three times a day if required
- Filgrastim SC once daily for 7 days from day 9

Extravasation risk:

Gemcitabine: non vesicant

Docetaxel: vesicant

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

Dosing in renal and hepatic impairment:

Renal	Gemcitabine	• CrCl>30ml/min – standard dosing • CrCl<30ml/min consider dose reduction (clinical decision)
	Docetaxel	No dose adjustment needed

Hepatic	Gemcitabine	Bilirubin < 27 µmol/L	100% dose
		Bilirubin ≥ 27 µmol/L	100% dose with active monitoring
	Docetaxel	AP ≤ 2.5 to 6 x ULN **AND** AST or ALT >1·5 to 10 x ULN	75%
		Bilirubin ≤ 1 to 1·5 x ULN:	50%
		Bilirubin > 1·5 x ULN **OR** AP > 6 x ULN **OR** AST/ALT > 10 x ULN	Not recommended

Interactions:

Gemcitabine

Yellow fever and other live attenuated vaccines are not recommended due to the risk of systemic, possibly fatal, disease, particularly in immunosuppressed patients

Docetaxel

In case of combination with CYP3A4 inhibitors, the occurrence of docetaxel adverse reactions may increase, as a result of reduced metabolism. If the concomitant use of a strong CYP3A4 inhibitor (e.g. ketoconazole, itraconazole, clarithromycin, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole) cannot be avoided, a close clinical surveillance is warranted and a dose-adjustment of docetaxel may be suitable during the treatment with the strong CYP3A4 inhibitor

Please refer to the SPC for more information

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Dexamethasone**	**8mg**	**PO**	30 minutes before chemotherapy
	Gemcitabine	**675mg/m^2**	**IV**	In 250mL 0.9% sodium chloride over 30 minutes
7	**Dexamethasone**	**8mg**	**PO**	Twice daily for 3 days starting 24 hours before docetaxel
8	**Gemcitabine**	**675mg/m^2**	**IV**	In 250mL 0.9% sodium chloride over 30 minutes
8	**Docetaxel**	**75mg/m^2**	**IV**	In 250mL 0.9% sodium chloride over 60 minutes

Main toxicities:

Gemcitabine	
Blood and lymphatic system disorders	Leucopenia Anaemia Bone marrow suppression
Respiratory	dyspnoea
Gastrointestinal disorders	Vomiting nausea
Hepatobillary disorders	Elevation of liver transaminases, increased bilirubin
Skin and subcutaneous tissue disorders	Allergic skin rash Alopecia itching
Docetaxel	
Blood and lymphaetic disorder	Neutropenia Anaemia
Metabolism and nutrition	Anorexia
Skin and subcutaneous disorders	Alopecia and nail disorders

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 1 D8	Cycle 2	Cycle 2 D8	Cycle 3	Cycle 3 D8	Ongoing
Informed Consent	X							
Clinical Assessment	X					X		As clinically indicated or at the end of treatment
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFTs & Magnesium	X	X	X	X	X	X	X	Every Cycle
CrCl (Cockcroft and Gault)	X	X		X		X		Every cycle
CT scan**	X					X		If clinically indicated
ECG								If clinically indicated
Main observations inc: blood pressure, respiratory rate	X	X	X	X	X	X	X	Every cycle
Height recorded	X							If clinically indicated
Weight recorded	X	X	X	X	X	X	X	Every cycle
Blood glucose	X							Repeat if clinically indicated

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

Proceed on day 8 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 75 x 10^9/L

Omit on day 8 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 74 x 10^9/L

On day 8 of the cycle if blood results do not meet the above levels the patient will miss that dose and proceed to the next cycle.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

If haematological recovery is delayed by more than 14 days, then reduce both gemcitabine and docetaxel by 20%.
If further delays then a second dose reduction of 20% should be applied.

Non- Haematological toxicity:

Day 1

Grade	Action
Grade 2	Omit until resolved then 100% dose
Grade 3	Omit until resolved then 80% dose
Grade 4	Omit until resolved then 50% dose- discuss with consultant

Pulmonary
Pulmonary symptoms of cough and breathlessness with chest X-ray evidence of infiltration have been noted with this combination. Acute admission and supportive care needed. Consider lung function tests. Severe impairment may require discontinuation of treatment but if symptoms improve consider proceeding.

References:

1. Summary product of characteristics. *Docetaxel* www.medicines.org.uk/emc/product/5762/smpc [Accessed on 17/05/2023]

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4. Fox E, Patel S, Wathen JK, Schuetze S, Chawla S, Harmon D, et al. Phase II Study of Sequential Gemcitabine Followed by Docetaxel for Recurrent Ewing Sarcoma, Osteosarcoma, or Unresectable or Locally Recurrent Chondrosarcoma: Results of Sarcoma Alliance for Research Through Collaboration Study 003. The oncologist. 2012;17(3):321-e9.
5. Mora J, Cruz CO, Parareda A, de Torres C. Treatment of relapsed/refractory pediatric sarcomas with Gemcitabine +/- docetaxel. Journal of pediatric hematology/oncology. 2009;31(10):723-9.
6. 1E.S. Rogers et al, Efficacy and safety of a single dose of dexamethasone pre docetaxel treatment: The Auckland experience Annals of Oncology (2014) 25 (suppl_4): iv517- iv541. 10.1093/annonc/mdu356

Circulation/Dissemination

Date added into Q-Pulse	For completion by DCM
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Version History

		Author name and designation	Summary of main changes

1.2	04/05/23	**Anna Burke (Pharmacist)**	Format Supportive meds Interaction Renal and hepatic impairment Main toxicity Haematological day 8
1.3	10/07/23	**Rob Challoner (Pharmacist)**	Simplified hepatic impairment dose reductions